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Richard C. Tilton

Microbiology

PreTest® Self-Assessment and Review

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Microbiology

PreTest® Self-Assessment and Review

Tenth Edition

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0-07-138970-9

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DOI: 10.1036/0071389709

Contents

Introduction . . . . . **vii**

High-Yield Facts

High-Yield Facts in Microbiology **1**

Virology

Questions **5**
Answers **32**

Bacteriology

Questions **55**
Answers **87**

Physiology and Molecular Microbiology

Questions **109**
Answers **129**

Rickettsiae, Chlamydiae, and Mycoplasmas

Questions **141**
Answers **149**

Mycology

Questions **155**
Answers **167**

Parasitology

Questions **177**
Answers **199**

Immunology

Questions **211**
Answers **240**

Bibliography **257**
Index **259**

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Introduction

Each *PreTest® Self-Assessment and Review* allows medical students to comprehensively and conveniently assess and review their knowledge of a particular basic science, in this instance microbiology. The 500 questions parallel the format and degree of difficulty of the questions found in the United States Medical Licensing Examination (USMLE) Step 1. Practicing physicians who want to hone their skills before USMLE Step 3 or recertification may find this to be a good beginning in their review process.

Each question is accompanied by an answer, a paragraph explanation, and a specific page reference to an appropriate textbook or journal article. A bibliography listing sources can be found following the last chapter of this text.

An effective way to use this PreTest® is to allow yourself one minute to answer each question in a given chapter. As you proceed, indicate your answer beside each question. By following this suggestion, you approximate the time limits imposed by the Step 1 exam.

After you finish going through the questions in the section, spend as much time as you need verifying your answers and carefully reading the explanations provided. Pay special attention to the explanations for the questions you answered incorrectly—but read *every* explanation. The authors of this material have designed the explanations to reinforce and supplement the information tested by the questions. If you feel you need further information about the material covered, consult and study the references indicated.

The High-Yield Facts added for this edition are provided to facilitate rapid review of microbiology. It is anticipated that the reader will use the High-Yield Facts as a "memory jog" before proceeding through the questions.

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High-Yield Facts in Microbiology

- Detection of HIV RNA by nucleic acid amplification of the viral load is the best predictor of "progression to AIDS." (Virology)
- HIV RNA PCR and sequencing of the amplified products may be used to monitor resistance to anti-HIV drugs. HIV patients with total CD4 lymphocyte counts of less than 200 CD4 cells/μL are susceptible to opportunistic infections such as those caused by *Cryptococcus, Mycobacterium,* and *Pneumocystis.* (Virology)
- *Cyclospora* is an ooidian parasite similar to *Cryptosporidium.* It causes food-borne diarrheal illness and has been associated with contaminated berries. (Parasitology)
- *Giardia,* a large flagellate with both cyst and trophozoite forms, is the most common parasitic disease in the United States. The disease is characterized by diarrhea, cramping, and fever. (Parasitology)
- Enterohemorrhagic *E. coli* causes bloody diarrhea and hemolytic uremic syndrome. The mode of action is production of Shiga-like toxin by *E. coli.* (Bacteriology)
- Vancomycin-resistant enterococci, methicillin-resistant *Staphylococcus aureus* (MRSA), and vancomycin-indeterminate *S. aureus* (VISA) are among the most feared nosocomial pathogens. A recently introduced antibiotic, quinapristin-delfapristin, effectively treats vancomycin-resistant enterococci or the few vancomycin-indeterminate MRSAs that have occurred. (Bacteriology)
- Following an upsurge of tuberculosis in the early 1990s, cases of *Mycobacterium tuberculosis* infection have remained static. *M. tuberculosis* causes initial primary pulmonary infection as well as a chronic disease characterized by hemoptysis, loss of weight, and fever. (Bacteriology)
- Penicillin-resistant pneumococci (*Streptococcus pneumoniae*) may account for up to 40% of isolates of *S. pneumoniae.* Third- or fourth-generation cephalosporins may be used as alternative treatment as well as vancomycin and rifampin. (Bacteriology)

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- *Ehrlichia,* a recently emerging tick-borne pathogen, is transmitted by *Ixodes scapularis,* the same tick that transmits the Lyme disease bacterium. *Ehrlichia* is also transmitted by the Lone Star tick, *Amblyomma americanum.* (*Chlamydia, Rickettsia*)
- Eastern equine encephalitis may be transmitted to humans by the bite of a mosquito, particularly in the northeastern United States. (Virology)
- Transfusion-associated babesiosis is a growing problem, particularly in the immunosuppressed or patients without a spleen. Tick-borne babesiosis caused by the same tick that transmits Lyme disease is an emerging infection. (Parasitology)
- Dengue fever, a viral illness transmitted by the *Aedes* mosquito, is prevalent in epidemic proportions in both the Caribbean and Southeast Asia. (Virology)
- There are five major classes of immunoglobulin: IgG, IgM, IgA, IgD, IgE. These immunoglobulins are distinguished by differences in the C regions of each individual H chain. These differences are function-related. (Immunology)
- Peptidoglycans are unique to prokaryotic organisms. They consist of a glycan backbone of muramic acid and glucosamine as well as cross-linked peptides. The enzymes responsible for cross-linking (transpeptidases) are the targets for β-lactam antibiotics. (Physiology)
- Genetic exchange in microorganisms occurs by several mechanisms, including transformation, transduction, conjugation, and transposition. These processes are the basis for gene cloning in microorganisms. (Physiology)
- Virulence factors in bacteria include adherence factors, invasins, capsules, endotoxin, and exotoxin. Such factors enable microorganisms to invade the host, cause disease, and resist host defense mechanisms. (Physiology)
- Sites of action of antimicrobial agents include cell-wall synthesis, cell membrane integrity, DNA replication, protein synthesis, DNA-dependent RNA polymerase, and folic acid metabolism. (Physiology)
- *Staphylococcus aureus* expresses two types of superantigens: enterotoxin (responsible for staphylococcal food poisoning) and toxic shock toxin. (Bacteriology)

- Free radicals of oxygen (superoxides) kill anaerobic bacteria exposed to air. Superoxide dismutase is a potent bacterial antioxidant. The presence of peroxidases in bacteria are protective. (Physiology)
- *Campylobacter* and *Helicobacter* are both helical-shaped bacteria. *Helicobacter* is known to play a role in the pathogenesis of peptic ulcer disease, while *Campylobacter* causes a food-borne gastrointestinal illness, most commonly from undercooked meat. Both bacteria are susceptible to antibiotics such as tetracycline. *Helicobacter* may be treated with Pepto-Bismol, metronidazole, and amoxicillin. (Bacteriology)
- The agents of bovine spongiform encephalopathy (Mad Cow Disease), scrapies, and new-variant Creutzfeldt-Jakob disease in humans are *prions* or amyloid fibrils. Also included are prions that cause chronic wasting disease (CWD) in elk and deer, although these agents of CWD have not been shown to be transmissable to either cattle or humans. These self-replicating proteins are resistant to heat and chemical agents. (Virology)
- Prior to 1999, West Nile virus, an arbovirus with serological cross-reactivity to St. Louis encephalitis virus was not seen in the United States. However, during 1999 and 2000, a large number of birds were infected with West Nile virus, as well as a few humans, some of whom died. (Virology)
- The genotype of hepatitis C is important in predicting the response of this virus to therapy with interferon and ribavirin as well as the required length of treatment. (Virology)

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Virology

Questions

DIRECTIONS: Each question below contains five suggested responses. Please choose the **one best** response to each question.

1. An HIV-positive patient asks you if you can tell him the chances of him progressing to symptomatic AIDS. Which one of the following tests would be most useful?

a. CD4 lymphocyte count
b. HIV antibody test
c. HIV RT PCR
d. Neopterin
e. HIV p24 antigen

2. Which of the following viruses causes an acute febrile rash and produces disease in immunocompetent children but has been associated with transient aplastic crises in persons with sickle cell disease?

a. Rubeola
b. Varicella-zoster
c. Parvovirus
d. Rubella
e. Herpes simplex

3. Infection with herpes simplex virus, a common human pathogen, is best described by which of the following statements?

a. The CNS and visceral organs are usually involved
b. It rarely recurs in a host who has a high antibody titer
c. It can be reactivated by emotional disturbances or prolonged exposure to sunlight
d. Initial infection usually occurs by intestinal absorption of the virus
e. Infection with type 1 virus is most common

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4. The latest and most effective therapy for AIDS patients includes azidothymidine (AZT), dideoxyinosine (DDI), and saquinavir or similar agents. Use of these three drugs would inhibit which of the following viral processes?

a. RNase, DNase
b. gp120 formation
c. p24 antibody expression
d. All membrane synthesis
e. Reverse transcriptase, protease

5. An HIV-positive patient prior to being treated with AZT, DDI, and saquinavir has a CD4 lymphocyte count and an HIV RNA viral load test done. Results are as follows:

CD4: 50 CD4 lymphocytes per microliter
HIV RNA: 750,000 copies per ml

Which of the following statements best describes the above patient?

a. This patient is no longer in danger of opportunistic infection
b. The 5-year prognosis is excellent
c. The patient's HIV screening test is most likely negative
d. The patient is not infectious
e. The viral load of 750,000 copies per ml suggests that the patient will respond to triple therapy

6. This HIV-positive patient with a viral load of 750,000 copies of HIV RNA/ml and a total CD4 count of 50 is at an increased risk for a number of infectious diseases. For which of the following diseases is the patient at no more added risk than an immunocompetent host?

a. Pneumocystic pneumonia
b. Mycobacterial disease
c. Kaposi's sarcoma
d. Pneumococcal pneumonia
e. Herpes simplex virus

7. Infectious mononucleosis, a viral disorder that can be debilitating, is characterized by which of the following statements?

a. It is most prevalent in children less than 14 years old
b. It is caused by a rhabdovirus
c. The causative pathogen is an Epstein-Barr virus
d. Affected persons respond to treatment with the production of heterophil antibodies
e. Ribavirin is the treatment of choice

8. A tube of monkey kidney cells is inoculated with nasopharyngeal secretions. During the next 7 days, no cytopathic effects (CPEs) are observed. On the eighth day, the tissue culture is infected accidentally with a picornavirus; nevertheless, the culture does not develop CPEs. The most likely explanation of this phenomenon is that

a. The nasopharyngeal secretions contained hemagglutinins
b. The nasopharyngeal secretions contained rubella virus
c. Picornavirus does not produce CPEs
d. Picornavirus does not replicate in monkey kidney cells
e. Monkey kidney cells are resistant to CPEs

9. The clinical picture of arbovirus infection fits one of three categories: encephalitis, hemorrhagic fever, or fever with myalgia. One of the characteristics of arboviruses is that they

a. Are transmitted by arthropod vectors
b. Are usually resistant to ether
c. Usually cause symptomatic infection in humans
d. Are closely related to parvoviruses

10. Which one of the following statements best describes interferon's suspected mode of action in producing resistance to viral infection?

a. It stimulates a cell-mediated immunity
b. It stimulates humoral immunity
c. Its direct antiviral action is related to the suppression of messenger RNA formation
d. Its action is related to the synthesis of a protein that inhibits translation or transcription
e. It alters the permeability of the cell membrane so that viruses cannot enter the cell

11. Coronaviruses are recognized by club-shaped surface projections that are 20 nm long and resemble solar coronas. These viruses are characterized by their ability to

a. Infect infants more frequently than adults
b. Cause the common cold
c. Grow well in the usual cultured cell lines
d. Grow profusely at 50°C
e. Agglutinate human red blood cells

12. Delta hepatitis only occurs in patients who also have either acute or chronic infection with hepatitis B virus. The delta agent is

a. An incomplete hepatitis B virus
b. Related to hepatitis A virus
c. A hepatitis B mutant
d. An incomplete RNA virus
e. Hepatitis C

13. Which of the following antiviral agents is a purine nucleoside analogue that has shown promise with Lassa fever, influenza A and B, and respiratory syncytial virus (RSV)?

a. Amantadine
b. Rimantadine
c. Vidarabine
d. Ribavirin
e. Acyclovir

14. Echoviruses are cytopathogenic human viruses that mainly infect the

a. Respiratory system
b. Central nervous system
c. Blood and lymphatic systems
d. Intestinal tract
e. Bladder and urinary tract

15. The most sensitive test for the diagnosis of herpes simplex (HSV) meningitis in a newborn infant is

a. HSV IgG antibody
b. HSV polymerase chain reaction (PCR)
c. HSV culture
d. Tzanck smear
e. Cerebrospinal fluid (CSF) protein analysis

16. Acute hemorrhagic conjunctivitis (AHC) is a contagious ocular infection characterized by pain, swelling of the eyelids, and subconjunctival hemorrhages. AHC has been reported to be caused by which of the following viruses?

a. Coronavirus
b. Reovirus
c. Rhinovirus
d. Enterovirus
e. Respiratory syncytial virus

17. Mumps virus accounts for 10 to 15% of all cases of aseptic meningitis in the United States. Infection with mumps virus

a. Is apt to recur periodically in many affected persons
b. Will usually cause mumps orchitis in postpubertal males
c. Is maintained in a large canine reservoir
d. Usually produces severe systemic manifestations
e. Is preventable by immunization

18. The serum of a newborn infant reveals a 1:32 cytomegalovirus (CMV) titer. The child is clinically asymptomatic. Which of the following courses of action would be advisable?

a. Repeat the CMV titer immediately
b. Wait 6 months and obtain another titer on the baby
c. Obtain a CMV titer from all siblings
d. Obtain an anti-CMV IgM titer from the mother
e. Obtain an anti-CMV IgM titer from the baby

19. A 3-year-old child presents at the physician's office with symptoms of coryza, conjunctivitis, low-grade fever, and Koplik's spots. The causative agent of this disease belongs to which group of viruses?

a. Adenovirus
b. Herpesvirus
c. Picornavirus
d. Orthomyxovirus
e. Paramyxovirus

20. One of the most common sexually transmitted diseases that may lead to cervical carcinoma is caused by which of the following viruses?

a. Cytomegalovirus
b. Papillomavirus
c. Epstein-Barr virus
d. Herpes simplex virus
e. Adenovirus

21. Which virus is the leading cause of the croup syndrome in young children and, when infecting mammalian cells in culture, will hemabsorb red blood cells?

a. Group B coxsackievirus
b. Rotavirus
c. Parainfluenza virus
d. Adenovirus
e. Rhinovirus

22. Hepatitis E, a recently characterized hepatitis virus, is best described by which of the following statements?

a. It is not a threat to the blood supply
b. It is a major cause of blood-borne hepatitis
c. It is prevalent in North America
d. It is a single-stranded DNA virus
e. The disease resembles hepatitis C

23. Meningitis is characterized by the acute onset of fever and stiff neck. Aseptic meningitis may be caused by a variety of microbial agents. During the initial 24 h of the course of aseptic meningitis, an affected person's cerebrospinal fluid is characterized by

a. Decreased protein content
b. Elevated glucose concentration
c. Lymphocytosis
d. Polymorphonuclear leukocytosis
e. Eosinophilia

24. Infection with hepatitis D virus (HDV; delta agent) can occur simultaneously with infection with hepatitis B virus (HBV) or in a carrier of hepatitis B virus because HDV is a defective virus that requires HBV for its replicative function. What serologic test can be used to determine whether a patient with HDV is an HBV carrier?

a. HBsAg
b. HBc IgM
c. HBeAg
d. HBs IgM
e. HBs IgG

25. A nurse develops clinical symptoms consistent with hepatitis. She recalls sticking herself with a needle approximately 4 months before after drawing blood from a patient. Serologic tests for HBsAg, antibodies to HBsAg, and hepatitis A virus (HAV) are all negative; however, she is positive for IgM core antibody. The nurse

a. Does not have hepatitis B
b. Has hepatitis A
c. Is in the late stages of hepatitis B infection
d. Is in the "window" (after the disappearance of HBsAg and before the appearance of anti-HBsAg)
e. Has hepatitis C

26. Eastern equine encephalitis virus is associated with a high fatality rate. Control of the disease could be possible by eradication of

a. Horses
b. Birds
c. Mosquitoes
d. Fleas
e. Ticks

27. Adults who have had varicella as children occasionally suffer a recurrent form of the disease, shingles. The agent causing these diseases is a member of which of the following viral families?

a. Herpesvirus
b. Poxvirus
c. Adenovirus
d. Myxovirus
e. Paramyxovirus

28. Rhinovirus is primarily transmitted by

a. Droplet aerosolization
b. Sexual activity
c. Fecal-oral route
d. Fomites
e. Vertical transmission from mother to child

29. German measles virus (rubella), a common cause of exanthems in children, is best described by which of the following statements?

a. Measles (rubeola) and German measles (rubella) are caused by the same virus
b. Incubation time is approximately 3 to 4 weeks
c. Vesicular rashes are characteristic
d. Onset is abrupt with cough, coryza, and fever
e. Specific antibody in the serum does not prevent disease

30. The presence of Negri inclusion bodies in host cells is characteristic of

a. Mumps
b. Infectious mononucleosis
c. Congenital rubella
d. Aseptic meningitis
e. Rabies

31. Kuru is a fatal disease of certain New Guinea natives and is characterized by tremors and ataxia; Creutzfeldt-Jakob disease (CJD) is characterized by both ataxia and dementia. These diseases are thought to be caused by

a. Slow viruses
b. Cell wall–deficient bacteria
c. Environmental toxins
d. Prions
e. Flagellates

32. According to recommendations issued by the U.S. Public Health Service, which of the following statements regarding vaccination against smallpox is true?

a. Pregnant women should be vaccinated in the first trimester
b. Persons who have eczema should be vaccinated soon after diagnosis
c. Persons who have immune deficiencies should be vaccinated every 5 years
d. Persons traveling abroad need not be vaccinated
e. Children should be vaccinated before they begin school

33. Hepatitis D virus (delta agent) is a defective virus that can replicate only in cells already infected with which of the following viruses?

a. Hepatitis A virus
b. Epstein-Barr virus
c. Hepatitis G virus
d. Hepatitis B virus
e. HIV

34. A patient presents with keratoconjunctivitis. The differential diagnosis should include infection with which of the following viruses?

a. Parvovirus
b. Adenovirus
c. Epstein-Barr virus
d. Respiratory syncytial virus
e. Varicella-zoster virus

35. A hospital worker is found to have hepatitis B surface antigen. Subsequent tests reveal the presence of e antigen as well. The worker most likely

a. Is infective and has active hepatitis
b. Is infective but does not have active hepatitis
c. Is not infective
d. Is evincing a biologic false-positive test for hepatitis
e. Has both hepatitis B and C

36. Alphavirus causes which one of the following viral diseases?

a. Marburg virus disease
b. St. Louis encephalitis
c. Western equine encephalitis
d. Dengue
e. Yellow fever

37. Several antiviral compounds have been developed during the last decade. One such compound is ribavirin, a synthetic nucleoside structurally related to guanosine. Ribavirin therapy has been successfully used against

a. Respiratory syncytial virus
b. Herpes simplex virus
c. Hepatitis B
d. Group A coxsackievirus
e. Parvovirus

38. An immunocompromised person with history of seizures had an MRI that revealed a temporal lobe lesion. Brain biopsy results showed multinucleated giant cells with intranuclear inclusions. The most probable cause of the lesion is

a. Hepatitis C virus
b. Herpes simplex virus
c. *Listeria monocytogenes*
d. Coxsackievirus
e. Parvovirus

39. Which of the following procedures or clinical signs is most specific for the diagnosis of infectious mononucleosis caused by the Epstein-Barr virus?

a. Laboratory diagnosis is based on the presence of "atypical lymphocytes" and EBV-specific antibody
b. Growth in tissue culture cells
c. Heterophile antibodies in serum
d. Lymphadenopathy and splenomegaly on physical examination
e. B-cell lymphocyte proliferation

40. An infant, seen in the ER, presents with a fever and persistent cough. Physical examination and a chest x-ray suggest pneumonia. Which of the following is most likely the cause of this infection?

a. Rotavirus
b. Adenovirus
c. Coxsackievirus
d. Respiratory syncytial virus
e. Rhinovirus

41. Which one of the following groups of people may be at increased risk for HIV infection?

a. Members of a household in which there is a person who is HIV-positive
b. Receptionists at a hospital
c. Factory workers whose coworkers are HIV-positive
d. Foreign service employees who are hospitalized in Zaire for bleeding ulcers
e. Homosexual females

42. An obstetrician sees a pregnant patient who was exposed to rubella virus in the eighteenth week of pregnancy. She does not remember getting a rubella vaccination. The best immediate course of action is to

a. Terminate the pregnancy
b. Order a rubella antibody titer to determine immune status
c. Reassure the patient because rubella is not a problem until after the thirtieth week
d. Administer rubella immune globulin
e. Administer rubella vaccine

43. Mad Cow Disease has been highly publicized in Great Britain. This disease, which is similar to scrapie, is caused by

a. A prion
b. A virus
c. *Rickettsiae*
d. An autoimmune reaction
e. A bacterium with a defective cell wall

44. A patient has all the gastrointestinal symptoms of infection with hepatitis A virus (HAV), yet all the tests for HAV-IgG and HAV-IgM are nonreactive. A possible cause of this infection is

a. Hepatitis B surface antigen
b. Hepatitis C
c. Hepatitis D
d. Hepatitis E
e. Rotavirus

45. A 70-year-old nursing home patient refused the influenza vaccine and subsequently developed influenza. She died of acute pneumonia 1 week after contracting the "flu." The most common cause of acute postinfluenzal pneumonia is

a. *Legionella*
b. *Listeria*
c. *Staphylococcus aureus*
d. *Klebsiella*
e. *Escherichia coli*

46. Which of the following viruses is primarily transmitted by the fecal-oral route?

a. St. Louis encephalitis virus
b. Colorado tick fever virus
c. Coxsackievirus
d. Yellow fever virus
e. Dengue fever virus

47. Hantavirus is an emerging pathogen that is best described by which of the following statements?

a. Influenza-like symptoms are followed rapidly by acute respiratory failure
b. Hemolysis is common in infected patients
c. It is acquired by inhalation of aerosols of the urine and feces of deer
d. Transmission from human to human is common
e. There is effective antiviral therapy available

48. Erythema infectiosum (fifth disease), a self-limited disease of children, is caused by

a. Measles
b. Parvovirus
c. Rubella
d. Human herpesvirus type 6
e. Norwalk virus

49. Which one of the following viruses may be human tumor virus?

a. Epstein-Barr virus (EBV)
b. HIV
c. Papillomavirus
d. Varicella-zoster virus (VZV)
e. Herpes simplex virus, type 2 (HSV)

50. Parvovirus infection, the cause of a mild exanthem in children, is characterized by

a. Epidemic acute respiratory disease
b. Gastroenteritis
c. Whooping cough–like disease
d. Keratoconjunctivitis
e. Acute hemolytic anemia

51. Cytomegalovirus (CMV) infection is common. Which one of the following statements best characterizes CMV?

a. It can be transmitted across the placental barrier
b. While a common infection, CMV is almost always symptomatic
c. The CMV can be cultured from red blood cells of infected patients
d. Unlike other viral infections, CMV is not activated by immunosuppressive therapy
e. There is no specific therapy for CMV

52. Human rotaviruses are characterized by which of the following statements?

a. They produce an infection that is primarily seen in adults
b. They produce cytopathic effects in many conventional tissue culture systems
c. They are lipid-containing RNA viruses possessing a double-shelled capsid
d. They can be sensitively and rapidly detected in stools by the enzyme-linked immunosorbent assay (ELISA) technique
e. They have been implicated as a major etiologic agent of infantile respiratory disease

53. Subacute sclerosing panencephalitis virus (SSPE) is best described by which of the following statements?

a. It is a progressive disease involving both white and gray matter
b. It is a late CNS manifestation of mumps
c. It is a common event occurring in 1 of 300,000 cases of mumps
d. Viral DNA can be demonstrated in brain cells
e. Demyelination is characteristic

54. Rotavirus is a double-stranded RNA virus with a double-walled capsid. Which one of the following statements best describes rotavirus?

a. There are no related animal viruses
b. It is a major cause of neonatal diarrhea
c. It is readily cultured from the stool of infected persons
d. Maternal antibody does not appear to be protective
e. Early breast-feeding offers no protection to neonates against it

55. Paramyxoviruses are most commonly associated with which of the following diseases?

a. Fifth disease
b. Rubella
c. Croup
d. Tonsillitis
e. Otitis media

56. Human papillomavirus is most commonly associated with

a. Rectal polyps
b. Prostate cancer
c. Condyloma acuminatum
d. Hepatic carcinoma
e. Carcinoma of the lung

57. Reverse transcriptase is an enzyme unique to the retroviruses. Which one of the following is a function of the enzyme reverse transcriptase?

a. DNase activity
b. RNA-dependent RNA polymerase activity
c. RNA isomerase activity
d. RNA-dependent DNA polymerase activity
e. Integration activity

58. St. Louis encephalitis, a viral infection, was first recognized as an entity in 1933. Which of the following best describes SLE?

a. It is transmitted to humans by the bite of an infected tick
b. It is caused by a togavirus
c. It is the major arboviral cause of central nervous system infection in the United States
d. It may present initially with symptoms similar to influenza
e. Laboratory diagnosis is routinely made by cultural methods

59. There is considerable overlap of signs and symptoms seen in congenital and perinatal infections. In a neonate with "classic" symptoms of congenital cytomegalovirus (CMV) infection, which one of the following tests would be most useful in establishing a diagnosis?

a. CMV IgG titer on neonate's serum at birth
b. CMV IgG titer on mother's serum at birth of infant
c. CMV IgM titer on neonate's serum at birth and at 1 month of age
d. Total IgM on neonate's serum at birth
e. Culture of mother's urine

60. Interferon, a protein that inhibits viral replication, is produced by cells in tissue culture when the cells are stimulated with which of the following?

a. Botulinum toxin
b. Synthetic polypeptides
c. Viruses
d. Chlamydiae
e. Gram-positive bacteria

61. Which one of the following statements best describes the cytopathic effects of viruses on host cells?

a. Usually morphological in nature
b. Often associated with changes in mitochondrial membranes
c. Pathognomonic for an infecting virus
d. Rarely fatal to the host cell
e. Can only be seen with an electron microscope

62. A 17-year-old girl presents with cervical lymphadenopathy, fever, and pharyngitis. Infectious mononucleosis is suspected. The most rapid and clinically useful test to make this diagnosis is

a. IgM antibody to viral core antigen (VCA)
b. IgG antibody to VCA
c. Antibody to Epstein-Barr nuclear antigen (EBNA)
d. Culture
e. C reactive protein (CRP)

63. Which one of the following viruses would be most likely to establish a latent infection?

a. Adenovirus
b. Measles virus
c. Influenza virus
d. Parvovirus
e. Coxsackievirus group B

64. A regimen that includes appropriately administered gamma globulin may be contraindicated in which one of the following diseases?

a. Hepatitis A
b. Hepatitis B
c. Rabies
d. Poliomyelitis
e. Infectious mononucleosis

65. Atypical lymphocytosis is most likely to be found in which one of the following diseases?

a. Encephalitis caused by herpes simplex virus (HSV)
b. Mononucleosis induced by Epstein-Barr virus
c. Parvovirus infection
d. Chronic hepatitis C
e. Rotavirus gastroenteritis

66. A patient has arthralgia, a rash, lymphadenopathy, pneumonia but no fever. Which of the following diseases is most likely based on these symptoms?

a. Dengue fever
b. St. Louis encephalitis
c. Infectious mononucleosis
d. Hepatitis
e. HIV infection

67. Hepatitis C (HCV) is usually a clinically mild disease, with only minimal elevation of liver enzymes. Hospitalization is unusual. Which one of the following statements best characterizes HCV?

a. Few cases progress to chronic liver disease
b. It often occurs in posttransfusion patients
c. HBV but not HCV infections occur in IV drug abusers
d. It is a DNA virus
e. Blood products are not tested for antibody to HCV

68. Which of the following markers is usually the first viral marker detected after hepatitis B infection?

a. HBeAg
b. HBsAg
c. HBcAg
d. Anti-HBc
e. HbeAb

69. Which of the following may be the only detectable serological marker during the early convalescent phase of HBV infection (window phase)?

a. HBeAg
b. HBsAg
c. HBcAg
d. Anti-HBc
e. HbeAb

70. Which one of the following markers is closely associated with HBV infectivity and DNA polymerase activity?

a. HBeAg
b. HBsAg
c. HBcAg
d. Anti-HBc
e. HBeAb

71. Which of the following is found within the nuclei of infected hepatocytes and not usually in the peripheral circulation?

a. HBeAg
b. HBsAg
c. HBcAg
d. Anti-HBc
e. HbeAb

72. Which one of the following viruses is the leading cause of congenital malformations?

a. Rabies
b. Rhinovirus
c. Cytomegalovirus
d. Respiratory syncytial virus
e. Mumps

73. Orchitis, which may cause sterility, is a possible manifestation of which of the following?

a. Rabies
b. Rhinovirus
c. Cytomegalovirus
d. Respiratory syncytial virus
e. Mumps

74. Which of the following is a leading cause of pneumonia primarily in infants?

a. Rabies
b. Rhinovirus
c. Cytomegalovirus
d. Respiratory syncytial virus
e. Mumps

75. Which of the following causes a fatal encephalitis for which a vaccine is available?

a. Rabies
b. Rhinovirus
c. Cytomegalovirus
d. Respiratory syncytial virus
e. Mumps

76. Traditional vaccination for the common cold is virtually impossible because there are multiple serotypes of which one of the following viruses?

a. Rabies
b. Rhinovirus
c. Cytomegalovirus
d. Respiratory syncytial virus
e. Mumps

77. Which of the following is available and effective for hepatitis A?

a. Acyclovir
b. Killed virus vaccine
c. Inactivated virus vaccine
d. Live virus vaccine
e. Recombinant viral vaccine

78. Patients should be vaccinated annually for influenza with which of the following vaccines?

a. Immune serum globulin
b. Killed virus vaccine
c. Inactivated virus vaccine
d. Live virus vaccine
e. Recombinant viral vaccine

79. The vaccine for measles is best characterized as a

a. Bacterin
b. Killed virus vaccine
c. Inactivated virus vaccine
d. Live virus vaccine
e. Recombinant viral vaccine

80. Which one of the following would be the treatment of choice for HSV infection?

a. Acyclovir
b. Killed virus vaccine
c. Herpes immune globulin
d. Azythromycin
e. Recombinant viral vaccine

81. Which of the following best describes the presently available vaccine for hepatitis B?

a. Synthetic peptide vaccine
b. Killed virus vaccine
c. Inactivated virus vaccine
d. Live virus vaccine
e. Recombinant viral vaccine

82. Chicken pox is a common disease of childhood. It is caused by which of the following viruses?

a. Cytomegalovirus
b. Rotavirus
c. Varicella-zoster virus
d. Adenovirus
e. Papillomavirus

83. Excluding influenza, which one of the following viruses is a common cause of acute respiratory disease?

a. Cytomegalovirus
b. Rotavirus
c. Varicella-zoster virus
d. Adenovirus
e. Papillomavirus

84. Human warts are not only cosmetically unsightly but may lead to cancer of the cervix. They are caused by which one of the following viruses?

a. Cytomegalovirus
b. Rotavirus
c. Varicella-zoster virus
d. Adenovirus
e. Papillomavirus

85. A vaccine is available for one of the most common causes of infantile gastroenteritis. However, it has recently been recalled. The virus is

a. Cytomegalovirus
b. Rotavirus
c. Varicella-zoster virus
d. Adenovirus
e. Papillomavirus

86. A child has mononucleosis-like symptoms yet the test for mononucleosis and the EBV titers are negative. One of the causes of heterophile-negative mononucleosis is

a. Cytomegalovirus
b. Herpes simplex virus
c. Varicella-zoster virus
d. Adenovirus
e. Coxsackievirus

87. Malaise and fatigue with increased "atypical" lymphocytes and a reactive heterophil antibody test is most commonly caused by

a. *Toxoplasma*
b. *Borrelia burgdorferi*
c. Epstein-Barr virus
d. Parvovirus
e. Rubella virus

88. Lethargy, malaise, and fatigue are observed in a patient 2 weeks after eating raw hamburger at a restaurant. The most likely infectious cause is

a. Toxoplasma
b. Cytomegalovirus
c. *E. coli*
d. Salmonella
e. Clostridium

89. Burkitt's lymphoma is characterized by elevated "early antigen" tests with a restricted pattern of fluorescence. This disease is caused by

a. Cytomegalovirus
b. *B. burgdorferi*
c. Epstein-Barr virus
d. *Lymphogranuloma venereum*
e. Herpes simplex virus

90. This virus may be detected by the polymerase chain reaction (PCR) in a variety of cells of patients with nasopharyngeal carcinoma.

a. Measles
b. Mumps
c. Rubella
d. Parvovirus
e. Epstein-Barr virus

91. This virus causes a mononucleosis-like syndrome caused by a latent herpesvirus; it is often a congenital infection. Large amounts of the virus are excreted in the urine; thus, urine becomes the fluid of choice for diagnosis of this disease.

a. Epstein-Barr virus
b. Cytomegalovirus
c. HHV-6
d. Parvovirus
e. Norwalk virus

Questions 92–96

Assume you are asked by a resident what the most appropriate specimen is for the detection of a particular virus.

92. Human papillomavirus

a. Cervical tissue
b. Synovial fluid
c. Blood
d. Skin

93. Cytomegalovirus

a. Cervical tissue
b. Synovial fluid
c. Blood
d. Skin
e. Cerebrospinal fluid

94. Enterovirus

a. Cervical tissue
b. Synovial fluid
c. Blood
d. Skin
e. Cerebrospinal fluid

95. Varicella-zoster virus (VZV)

a. Cervical tissue
b. Synovial fluid
c. Blood
d. Skin
e. Cerebrospinal fluid

96. Adenovirus 40/41

a. Cervical tissue
b. Synovial fluid
c. Blood
d. Stool
e. Cerebrospinal fluid

97. Which of the following is transmitted by the fecal-oral route; can be acquired from shellfish; and often causes acute jaundice, diarrhea, and liver function abnormalities?

a. Rotavirus
b. Adenovirus 40/41
c. Norwalk virus
d. Astrovirus
e. Hepatitis A virus

98. Which of the following is the second most common cause of pediatric gastroenteritis? Unlike other similar viruses, this virus causes only gastroenteritis.

a. Rotavirus
b. Adenovirus 40/41
c. Norwalk virus
d. Astrovirus
e. Hepatitis A virus

99. Which of the following is the most common cause of pediatric gastroenteritis? It is difficult to grow in cell culture but can be detected easily by immunologic methods (ELISA).

a. Rotavirus
b. Adenovirus 40/41
c. Norwalk virus
d. Astrovirus
e. Hepatitis A virus

100. Which of the following is a common cause of epidemic gastroenteritis, particularly aboard cruise ships and in summer camps? It may be detected by ELISA methods or electron microscopy.

a. Rotavirus
b. Adenovirus 40/41
c. Norwalk virus
d. Astrovirus
e. Hepatitis A virus

101. Which of the following is a cause of mild gastroenteritis? It can be transmitted by the fecal-oral route but not by food consumption.

a. Rotavirus
b. Adenovirus 40/41
c. Norwalk virus
d. Astrovirus
e. Hepatitis A virus

102. IgM antibody to the viral particle is the method of choice for laboratory diagnosis of which one of the following hepatitis viruses?

a. Hepatitis A
b. Hepatitis B
c. Hepatitis C
d. Hepatitis D
e. Hepatitis E

103. This virus belongs to the family of flaviviruses and its reservoir is strictly human. Transmission is blood-borne so the blood supply is routinely screened for this virus.

a. Hepatitis A
b. Hepatitis B
c. Hepatitis C
d. Hepatitis D
e. Hepatitis E

104. Vaccination for this hepatic disease is with viral surface antigen and usually provides immunity.

a. Hepatitis A
b. Hepatitis B
c. Hepatitis C
d. Hepatitis D
e. Hepatitis E

105. This hepatitis virus is a calicivirus. The reservoir is in pigs, and humans acquire it via the fecal-oral route.

a. Hepatitis A
b. Hepatitis B
c. Hepatitis C
d. Hepatitis D
e. Hepatitis E

106. This hepatitis virus is a defective virus in that it cannot replicate independently without the presence of hepatitis B virus.

a. Hepatitis A
b. Hepatitis B
c. Hepatitis C
d. Hepatitis D
e. Hepatitis E

107. Which of the following is the causative agent of a variety of cutaneous warts (plantar, common, and flat) and is associated with cervical neoplasia?

a. Human papillomavirus
b. West Nile virus
c. Tick-borne encephalitis virus
d. *Polyomavirus*
e. Subacute sclerosing panencephalitis virus (SSPE)

108. Recently appearing in the United States, this virus is carried by birds, transmitted by mosquitoes, and infects humans and horses.

a. Human papillomavirus
b. West Nile virus
c. Tick-borne encephalitis virus
d. *Polyomavirus*
e. SSPE

109. Which of the following viruses causes progressive multifocal leukoencephalopathy (PML), a disease causing demyelination in the central nervous system?

a. Human papillomavirus
b. West Nile virus
c. Tick-borne encephalitis virus
d. *Polyomavirus*
e. SSPE

110. This virus is transmitted by the same arthropod that transmits babesiosis and ehrlichiosis.

a. Human papillomavirus
b. West Nile virus
c. Tick-borne encephalitis virus
d. *Polyomavirus*
e. SSPE

111. This virus is a single-stranded RNA orthomyxovirus. Annual vaccination is necessary because of antigenic drift and shift.

a. Measles virus
b. Influenza virus
c. Respiratory syncytial virus
d. Parainfluenza virus
e. Adenovirus

112. This virus is a single-stranded RNA paramyxovirus. The rash known as Koplik's spots is pathognomonic.

a. Measles virus
b. Influenza virus
c. Respiratory syncytial virus
d. Parainfluenza virus
e. Adenovirus

113. This virus is the leading cause of bronchiolitis and community-acquired pneumonia in infants.

a. Measles virus
b. Influenza virus
c. Respiratory syncytial virus
d. Parainfluenza virus
e. Adenovirus

114. This is a paramyxovirus and causes the syndrome known as croup.

a. Measles virus
b. Influenza virus
c. Respiratory syncytial virus
d. Parainfluenza virus
e. Adenovirus

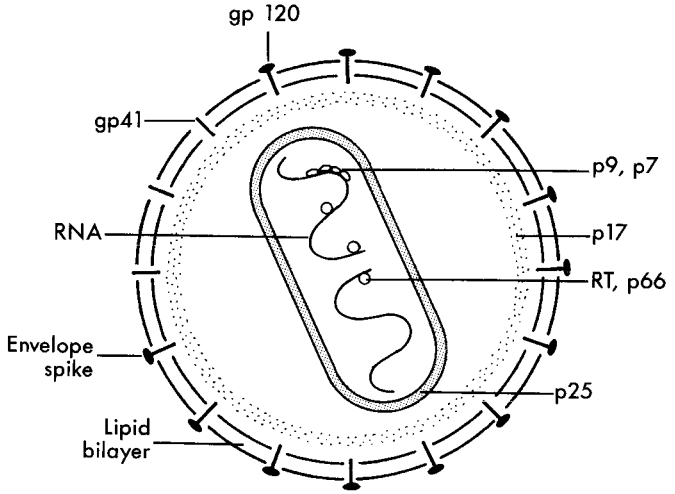
115. This is a double-stranded DNA virus. It is responsible for 15% of pediatric respiratory infections and 10 to 15% of acute diarrhea in children.

a. Measles virus
b. Influenza virus
c. Respiratory syncytial virus
d. Parainfluenza virus
e. Adenovirus

Virology

Answers

1. The answer is c. *(Ryan, pp 552–554.)* HIV RT PCR, a nucleic acid amplification test for HIV RNA, has recently been shown to be the most valuable test for a) monitoring a patient's progress during triple drug therapy and b) determining the chances of progression to AIDS. A viral load of 750,000 copies per ml significantly increases the chance of progression to AIDS within 5 years. The other tests listed do not accurately predict progression to AIDS. The figure below shows the basic structure of HIV including the enzyme, reverse transcriptase.



The location of the envelope glycoproteins (gp120 and gp124) is shown, as are the major viral core proteins (p25, p17, p9, and p7). The core protein, p17, is found outside the viral nucleoid and forms the matrix of the virion. RT indicates reverse transcriptase.

2. The answer is c. *(Davis, pp 927–928. Raoult, p 785.)* Parvovirus B 19 is the causative agent of erythema infectiosum (fifth disease). It is associated with transient aplastic crisis in persons with hereditary hemolytic anemia. In adults, it is also associated with polyarthralgia.

3. The answer is c. *(Davis, p 935. Raoult, pp 470–474.)* The initial infection by herpes simplex virus is often inapparent and occurs through a break in the skin or mucous membranes, such as in the eye, throat, or genitals. Latent infection often persists at the initial site despite high antibody titers. Recurrent disease can be triggered by temperature change, emotional distress, and hormonal factors. Type 1 herpes simplex virus is usually, but not exclusively, associated with ocular and oral lesions; type 2 is usually, but not exclusively, associated with genital and anal lesions. Type 2 infection is more common. In addition to mucocutaneous infections, the CNS and occasionally visceral organs can be involved.

4–6. The answers are 4-e, 5-e, 6-d. *(Levinson, pp 271–279.)* The advent of triple therapy or a therapeutic "cocktail" has had a marked effect on AIDS patients. The combination of drugs work together as reverse transcriptive inhibitors and a protease inhibitor. Patients improve rapidly, their CD4 lymphocyte counts increase, and their HIV viral load is drastically reduced, often to <50 copies per ml. On the other hand, an untreated HIV-positive patient with a low CD4 and a high viral load a) is at increased risk of opportunistic infection and b) has a much greater chance of developing AIDS than if the viral load was <50,000. The patient is infectious and his HIV antibody screening test will be positive. The high viral load, however, is not a predictor of response to therapy. Many patients with high viral loads do very well on triple therapy, although resistance to one or more of the agents may subsequently occur. A low CD4 count does not predict progression to AIDS but does indicate increased chance of opportunistic infection such as those listed. Kaposi's sarcoma, which has been linked to herpesvirus type 8, pneumocystis, and mycobacterial disease are three of the most prevalent opportunistic infections. While HIV-positive patients contract pneumococcal pneumonia, they are probably at no more risk than the general population, as protection against pneumococcal disease is linked to the presence of anticapsular antibody.

7. The answer is c. *(Murray, pp 912–918.)* All of Koch's postulates have been verified for the relationship between infectious mononucleosis and Epstein-Barr virus, a herpesvirus. However, the relationship between this virus and Burkitt's lymphoma, sarcoid, and systemic lupus erythematosus (SLE) is less clear. Infectious mononucleosis is most common in young adults (14 to 18 years of age) and is very rare in young children. There is

no specific treatment. Heterophil antibody titer is helpful in diagnosis, but is not expressed as a function of clinical recovery.

8. The answer is b. *(Levinson, pp 231–232.)* Rubella virus does not produce cytopathic effects (CPEs) in tissue-culture cells. Moreover, rubella-infected cells challenged with a picornavirus are resistant to subsequent infection and thus would not exhibit CPEs. Monkey kidney cells infected only with picornavirus would show CPEs.

9. The answer is a. *(Levinson, pp 252–256.)* Arboviruses (arthropod-borne viruses) may or may not be surrounded by a lipid envelope, although most are inactivated by lipid solvents such as ether and may contain either double-stranded or single-stranded RNA. Physicochemical studies have demonstrated a great heterogeneity among these viruses. Arboviruses cause disease in vertebrates; in humans, encephalitis is a frequent arbovirus illness. Most human infections with arbovirus, however, are asymptomatic.

10. The answer is d. *(Levinson, pp 190–191.)* Interferon is a protein produced by cells in response to a viral infection or certain other agents. Entering uninfected cells, interferon causes production of a second protein that alters protein synthesis. As a result of inhibition of either translation or transcription, new viruses are not assembled following infection of interferon-protected cells.

11. The answer is b. *(Raoult, p 250.)* Coronaviruses, discovered in 1965, are thought to be a major agent of the common cold, especially in older children and adults. The virion is known to contain RNA, but other elements of its structure are unclear. At 34°C, viral multiplication is profuse; however, infectivity is greatly reduced at higher temperatures or following extended incubation.

12. The answer is d. *(Levinson, pp 249–250.)* The delta agent was first described in 1977 and has recently been shown to be an incomplete RNA virus that requires HBsAg for replication. It is found most often in persons who have multiple parenteral exposures, for example, intravenous (IV) drug abusers, hemophiliacs, and multiply transfused patients.

13. The answer is d. *(Raoult, pp 555–557.)* As an intravenous agent, ribavirin is effective against Lassa fever in the first week of onset of the disease. It may also be administered as an aerosol that is quite useful in infants with RSV. Unlike amantadine, which is efficacious only with influenza A, ribavirin has activity against both influenza A and B if administered by aerosol in the first 24 h of onset.

14. The answer is d. *(Levinson, p 239.)* Echoviruses were discovered accidentally during studies on poliomyelitis. They were named *enteric cytopathogenic human orphan* (*ECHO*) *viruses* because, at the time, they had not been linked to human disease and thus were considered "orphans." Echoviruses now are known to infect the intestinal tract of humans; they also can cause aseptic meningitis, febrile illnesses, and the common cold. Echoviruses range in size from 24 to 30 nm in diameter and contain a core of RNA.

15. The answer is b. *(Levinson, pp 208–216.)* HSV meningitis or encephalitis is difficult to diagnose by laboratory tests as there is a low titer of virus present in the CSF. Neonatal HSV infects the child during the birth process. While culture, Tzanck smear, and even antibody tests may be useful in adults, particularly those with HSV-rich lesions, they are not useful for CSF testing. Only PCR is sensitive enough to detect HSV DNA in the CSF. Once diagnosed rapidly, HSV encephalitis or meningitis can be treated with acyclovir.

16. The answer is d. *(Levinson, pp 238–239.)* Enterovirus and Coxsackievirus A can be recovered from conjunctival scrapings of patients with acute hemorrhagic conjunctivitis (AHC) during the first 3 days of illness. Isolation rates are somewhat higher for enterovirus than Coxsackievirus. Less than 5% of throat swab or fecal specimens have been positive for either virus.

17. The answer is e. *(Levinson, pp 228–229.)* Much of the public's understanding of mumps is based on suppositions that are without any scientific basis. For example, natural mumps infection confers immunity after a single infection, even if the infection was a unilateral, not bilateral, parotitis. Also, sterility from mumps orchitis is not assured; only 20% of males older than 13 years of age develop orchitis. The majority of patients with mumps do not develop systemic manifestations. In fact, some do not develop

parotitis. Last, the virus is maintained exclusively in human populations; canine reservoirs are not known. The mumps vaccine is a live attenuated virus vaccine derived from chick-embryo tissue culture.

18. The answer is e. *(Levinson, pp 213–214.)* Clinical manifestations of cytomegalovirus (CMV) infection may not be readily apparent at birth. Thus, in a newborn infant with a 1:32 titer of CMV, it is necessary to determine whether the antibodies were passed transplacentally from the mother (these antibodies would be IgG) or produced by the fetus in response to an in utero infection (IgM). A newborn infant who is infected excretes large numbers of virus particles in the urine and, therefore, places other neonates at risk for contracting CMV disease.

19. The answer is e. *(Raoult, pp 619–628.)* Koplik's spots are pathognomonic for measles. The measles virus is a paramyxovirus. In industrialized countries, vaccination has reduced the importance of this childhood infection (although U.S. incidence increased in 1989 and 1990). In developing countries, however, measles is a major killer of young children. In America, most states now require proof of immunity before school enrollment, and this has reduced the incidence of disease.

20. The answer is b. *(Levinson, pp 219–220.)* Human papillomavirus (HPV) is the cause of genital warts. It is one of the most pervasive of all the sexually transmitted diseases. There is no specific cure or vaccine. There are multiple serotypes of papillomavirus and some serotypes are linked to cervical cancer. New techniques for molecular diagnosis of HPV show promise for rapid and sensitive detection and perhaps more aggressive treatment.

21. The answer is c. *(Levinson, pp 230–231.)* Parainfluenza viruses are important causes of respiratory diseases in infants and young children. The spectrum of disease caused by these viruses ranges from a mild febrile cold to croup, bronchiolitis, and pneumonia. Parainfluenza viruses contain RNA in a nucleocapsid encased within an envelope derived from the host cell membrane. Infected mammalian cell culture will hemabsorb red blood cells owing to viral hemagglutinin on the surface of the cell.

22. The answer is a. *(Levinson, pp 250–251.)* Hepatitis E is a newly recognized single-stranded RNA virus in the calicivirus family. Epidemics

have been observed in Asia, Africa, India, and Mexico. Like HAV, it is enterically transmitted but there is no vaccine available nor routine detection test. Chronic liver disease does not occur, and because it is not blood-borne it is of no threat to the blood supply.

23. The answer is d. *(Levinson, pp 238–239.)* Aseptic meningitis is characterized by a pleocytosis of mononuclear cells in the cerebrospinal fluid; polymorphonuclear cells predominate during the first 24 h, but a shift to lymphocytes occurs thereafter. The cerebrospinal fluid of affected persons is free of culturable bacteria and contains normal glucose and slightly elevated protein levels. Peripheral white blood cell counts usually are normal. Although viruses are the most common cause of aseptic meningitis, spirochetes, chlamydiae, and other microorganisms also can produce the disease.

24. The answer is b. *(Levinson, pp 189, 206, 246.)* In a chronic HBV carrier, there would be no HB core IgM antibody, whereas it would be present in a new HBV infection. The HBe antigen could be present in either an HBV carrier or in acute infection. HBsAg would be present in either a new infection or in the carrier state, while HBsAb would not be present in either case.

25. The answer is d. *(Levinson, pp 243–247.)* In a small number of patients with acute hepatitis B infection, HBsAg can never be detected. In others, HBsAg becomes negative before the onset of the disease or before the end of the clinical illness. In such patients with acute hepatitis, hepatitis B virus infection may only be established by the presence of anti-hepatitis B core IgM (anti-HBc IgM), a rising titer of anti-HBc, or the subsequent appearance of anti-HBsAg.

26. The answer is c. *(Levinson, pp 253–254.)* Eastern equine encephalitis (EEE) is a severe disease usually seen in the summer months when *Aedes* mosquitoes are prevalent. In 1996 and 1997, there were several outbreaks in the Northeast United States. Control of EEE is a function of mosquito eradication. Horses and humans are accidental hosts. While draining of swamps helps, other measures to eliminate mosquitoes such as spraying are the most effective.

27. The answer is a. *(Levinson, pp 212–213.)* Varicella-zoster virus, a member of the herpesvirus group, causes a usually mild, self-limited illness

in children. Recurrent disease in adults who possess circulating antibody against varicella-zoster virus may be more severe and cause an inflammatory reaction in the sensory ganglia of spinal or cranial nerves. This disease, shingles, appears to result from the reactivation (by trauma or other stimuli) of latent varicella-zoster virus.

28. The answer is d. *(Levinson, pp 239–240.)* Rhinovirus is a major cause of the common cold. The primary mode of transmission is the contact of contaminated hands, fingers, or fomites with the conjunctiva or nasal epithelium. While several studies have shown no evidence of aerosol transmission, a study by Dick and associates in 1986 did show aerosol transmission can occur. This is not, however, the main mode of transmission.

29. The answer is d. *(Levinson, pp 227–228.)* Measles (rubeola) is an acute, highly infectious disease characterized by a maculopapular rash. German measles (rubella) is an acute, febrile illness characterized by a rash as well as suboccipital lymphadenopathy. Incubation time is 9 full days after exposure. Onset is abrupt and symptoms mostly catarrhal. Koplik's spots, pale, bluish-white spots in red areolas, can frequently be observed on the mucous membranes of the mouth and are pathognomonic for measles.

30. The answer is e. *(Levinson, pp 232–234.)* The definitive diagnosis of rabies in humans is based on the finding of Negri bodies, which are cytoplasmic inclusions in the nerve cells of the spinal cord and brain, especially in the hippocampus. Negri bodies are eosinophilic and generally spherical in shape; several may appear in a given cell. Negri bodies, although pathognomonic for rabies, are not found in all cases of the disease.

31. The answer is d. *(Levinson, pp 268–271.)* Kuru and Creutzfeldt-Jakob disease (CJD) are similar but not identical diseases with very different epidemiology. Kuru is prevalent among certain tribes in New Guinea who practiced ritual cannibalism by eating the brains of the departed. CJD is found worldwide and has been transmitted by corneal transplants and in pituitary hormone preparations. There is some association between CJD and Mad Cow Disease in England. Prions are unconventional self-replicating proteins, sometimes called amyloid. It is now thought that CJD, Kuru, and animal diseases such as scrapie, visna, and bovine spongiform encephalopathy (Mad Cow Disease) are caused by prions.

32. The answer is d. *(Levinson, pp 216–217.)* Routine vaccination of infants and children for smallpox has been discontinued in the United States, both because the risk of contracting the disease is so low and because the complications of smallpox vaccination, including generalized vaccinia eruption, postvaccinal encephalitis, and fetal vaccinia, are significant. Owing to the extremely effective eradication of smallpox worldwide by the World Health Organization, U.S. citizens traveling abroad no longer require vaccination. Pregnancy, immune deficiencies, and eczema and other chronic dermatitides are contraindications to smallpox vaccination.

33. The answer is d. *(Ryan, pp 422–500.)* Hepatitis D virus is a defective virus with an RNA genome and a hepatitis B surface antigen envelope. Two types of HDV infection occur: simultaneous HDV and HBV infection, or HDV superinfection with chronic HBV infection. Diagnosis is made by demonstrating IgM or IgG antibodies, or both.

34. The answer is b. *(Levinson, pp 218–219.)* Adenovirus type 8 is associated with epidemic keratoconjunctivitis, while adenovirus types 3 and 4 are often associated with "swimming pool conjunctivitis." There are also reports of nosocomial conjunctivitis with adenovirus. Herpes simplex virus can infect the conjunctiva and is among the most common causes of blindness in North America and Europe.

35. The answer is a. *(Levinson, pp 243–246.)* The e antigen seems to be related to the Dane particle, which is presumed to be the intact hepatitis B virus. Possession of the e antigen suggests active disease and, thus, an increased risk of transmission of hepatitis to others. HBsAg and e antigen are components of hepatitis B and are not shared by other hepatitis viruses.

36. The answer is c. *(Levinson, pp 253–255.)* St. Louis encephalitis, yellow fever, and dengue are caused by flaviviruses. Western equine encephalitis is caused by an alphavirus. Laboratory diagnosis is usually made by demonstration of a fourfold rise in specific antibody titer in paired sera.

37. The answer is a. *(Levinson, p 201.)* Ribavirin is effective to varying degrees against several RNA- and DNA-containing viruses in vitro. It has been approved for aerosol treatment of respiratory syncytial virus infec-

tions in infants. Intravenous administration has proved effective in treating Lassa fever.

38. The answer is b. *(Ryan, p 505.)* Herpes simplex virus causes primary and recurrent disease. The typical skin lesion is a vesicle that contains virus particles in serous fluid. Giant multinucleated cells are typically found at the base of the herpesvirus lesion. Encephalitis, which usually involves the temporal lobe, has a high mortality rate. Severe neurologic sequelae are seen in surviving patients.

39. The answer is b. *(Ryan, pp 514–515.)* Contact with infected secretions such as saliva can result in infection with EBV, thus the term *kissing disease*. Laboratory diagnosis of EBV-induced infectious mononucleosis is usually determined by presence of atypical lymphocytes, heterophile antibodies, or specific antiviral antibodies such as VCA (viral capsid antibody).

40. The answer is d. *(Baron, pp 731–732.)* Respiratory syncytial virus (RSV) is the most important cause of pneumonia and bronchiolitis in infants. The infection is localized to the respiratory tract. The virus can be detected rapidly by immunofluorescence on smears of respiratory epithelium. In older children, the infection resembles the common cold. Aerosolized ribavirin is recommended for severely ill hospitalized infants.

41. The answer is d. *(Howard, pp 838–840.)* Many believe that casual contact with patients who are HIV-positive increases the risk of acquiring the disease. This is not the case. It is also clear that homosexual females have a low rate of HIV acquisition. Because a substantial portion of the blood supply in Central African countries is HIV-infected, hospitalization is risky particularly if transfusion is necessary.

42. The answer is b. *(Howard, pp 819–821.)* The highest risk of fetal infection with rubella occurs during the first trimester. In seronegative patients, the risk of infection exceeds 90%. However, before other measures (such as termination of pregnancy) are considered, a rubella immune status must be performed. A rubella titer of 1:10 is protective.

43. The answer is a. *(Howard, pp 755–756.)* Mad Cow Disease is related to both scrapie in sheep and bovine spongiform encephalopathy virus. The

fear in Great Britain is the potential for acquiring Creutzfeldt-Jakob disease, which is a slowly progressive neurodegenerative disease. Theoretically, such acquisition could be through ingestion of beef from infected cows. A prion consists of protein material without nucleic acid. While related to a virus, a prion is a proteinaceous infectious particle that replicates within cells.

44. The answer is d. *(Howard, pp 755–756.)* Hepatitis E virus (HEV) is a single-stranded RNA virus. It is transmitted enterically, and the disease is often referred to as *enteric hepatitis C.* There is no test for HEV routinely available. Diagnosis is clinical and also one of exclusion.

45. The answer is c. *(Levinson, pp 47, 87.) Staphylococcus aureus* is the most common cause of postinfluenzal secondary bacterial pneumonia. It most often affects the elderly, although patients of any age may be afflicted. The pneumococcus as well as group A streptococci and *Haemophilus influenzae* may also cause pneumonia.

46. The answer is c. *(Levinson, pp 253–256.)* St. Louis encephalitis virus is spread by mosquitoes and causes a severe encephalitis with a near 10% fatality rate. Colorado tick fever, spread by the wood tick, causes fever, headache, retro-orbital pain, and severe myalgia. Fever and jaundice characterize yellow fever, a life-threatening disease spread by mosquitoes. Following fever, headache, myalgias, and photophobia, the symptoms progress to the liver, kidney, and heart. Mortality rate is high. Dengue fever shares the same mosquito vector as yellow fever. Classic dengue fever (breakbone fever) includes flu-like symptoms. Severe muscle and joint (breakbone) pain occurs. Coxsackievirus is spread by the fecal-oral route.

47. The answer is a. *(Levinson, p 280.)* In 1993, an outbreak of a fatal respiratory disease occurred in the southwestern United States. This disease is caused by a Hantavirus endemic in deer mice. It is not transmitted from person to person. The mortality rate is 60%. Ribavirin has been used but is not effective. A vaccine is not available.

48. The answer is b. *(Levinson, pp 221–222.)* Parvovirus B19 causes the common disease erythema infectiosum, characterized by a "slapped cheek" rash. Called *fifth disease,* it is the fifth childhood rash disease; the other four are measles, rubella, scarlet fever, and roseola.

49. The answer is c. *(Levinson, pp 257–267.)* Only two human viruses have been confirmed as human tumor viruses. They include human T-cell lymphoma/leukemia virus (HTLV) and papillomavirus. Others, such as EBV, HSV, and hepatitis B and C, have been implicated as tumor viruses. The virus that causes chicken pox (VZV) is not know to be oncogenic.

50. The answer is e. *(Howard, pp 781–783.)* Adenoviruses are widespread and cause a variety of clinical problems. Many of the "viral sore throats" among young people living in close quarters are due to adenovirus. Parvovirus B19, not adenovirus, causes acute hemolytic anemia.

51. The answer is a. *(Davis, pp 1071–1073. Tilton, 276–278.)* Although infection with cytomegalovirus (CMV) is common, it only rarely causes clinically apparent disease. Lesions characteristic of infection with CMV are found in up to 10% of stillborn babies; however, CMV, which can be transmitted transplacentally, usually is not the cause of death. Children and adults with immunosuppressive problems are susceptible to active disease. In severely immunodeficient patients such as those with AIDS, CMV ocular disease may occur. The patient suffers blurring of vision or vision loss, and ophthalmic examination reveals large yellowish-white areas with flame-shaped hemorrhages. Ganciclovir is now licensed for treatment of CMV retinitis in AIDS patients.

52. The answer is d. *(Levinson, pp 240–241.)* Rotaviruses were initially identified by direct electron microscopy (EM) of duodenal mucosa of infants with gastroenteritis. Subsequent studies in several countries have shown them to be the cause of 30 to 40% of acute diarrhea in infants. They are non-lipid-containing RNA viruses with a double-shelled capsid. Although the virus has been serially propagated in human fetal intestinal organ cultures, cytopathic changes are minimal or absent; multiplication is detected by immunofluorescence. Numerous methods for rotavirus antigen detection, including radioimmunoassay, counterimmunoelectrophoresis, and enzyme-linked immunosorbent assay, have been developed and found to be about as effective as EM.

53. The answer is a. *(Levinson, pp 268–269.)* SSPE is a late and rare manifestation of measles. It is a progressive encephalitis involving both white and gray matter. Demyelination is seen only at an advanced stage of the dis-

ease in a few cases. In 1985, viral RNA was demonstrated in brain cells from a patient with SSPE by the use of in situ hybridization.

54. The answer is b. *(Howard, pp 834–835.)* Rotavirus is a viral entity that is similar to Nebraska calf diarrhea virus and is thought to be a major cause of acute diarrhea in newborn infants. Three-quarters of all adults have antibodies against rotavirus; passive transfer of these antibodies to the baby, especially through the colostrum, seems to be protective. Although vaccination would be expected to be of little use to the neonate, it might effectively immunize pregnant mothers.

55. The answer is c. *(Levinson, pp 226–231.)* Both mumps and measles are well-recognized paramyxovirus infections. This group also includes parainfluenza virus, which causes laryngotracheobronchitis (croup) in children, and respiratory syncytial virus, which can cause bronchiolitis in infants. Paramyxoviruses have glycoprotein spikes that extend their lipid membrane and are responsible for hemagglutination activities.

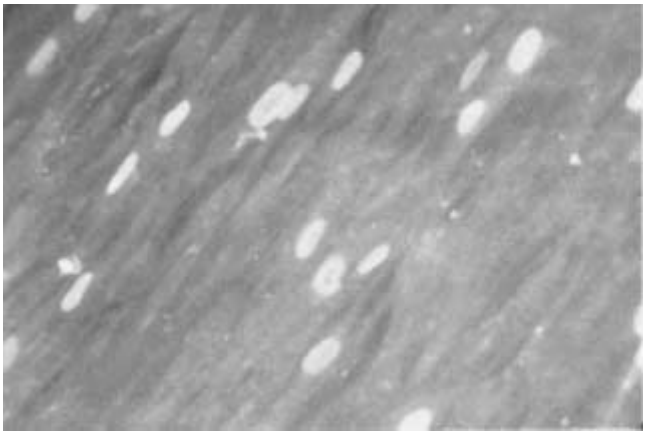
56. The answer is d. *(Levinson, pp 219–220.)* Papillomavirus infects the skin or mucosa and causes benign tumors. The lesion is termed condyloma acuminatum. These tumors may undergo malignant conversion and become squamous cell carcinomas. Classification of the human papillomavirus is done by DNA hybridization, and to date 46 types have been recognized. Some types, such as 16 and 18, are more frequently associated with carcinoma, while others, such as 6 and 11, are associated with benign tumors or warts.

57. The answer is d. *(Raoult, p 482.)* The replication of a retroviral genome is dependent on the reverse transcriptase enzyme, which performs a variety of functions. It builds a complementary strand of DNA for the viral RNA template; it builds a second DNA strand complementary to the previous DNA; it degrades the original RNA, leaving a DNA-DNA duplex; and, finally, it is responsible for integrating the new viral DNA hybrid into the host genome.

58. The answer is c. *(Levinson, p 254.)* St. Louis encephalitis virus has structural and biologic characteristics in common with other flaviviruses. It is the most important arboviral disease in North America. St. Louis

encephalitis virus was first isolated from mosquitoes in California. Patients who contract the disease usually present with one of three clinical manifestations: febrile headache, aseptic meningitis, or clinical encephalitis.

59. The answer is c. *(Howard, pp 791–793.)* (See figure below.) Presently, cytomegalovirus (CMV) is the most common cause of congenital and perinatal viral infections. Culture of the virus is a sensitive diagnostic technique; in the case of a neonate with classic symptoms, serum samples from the mother and neonate are obtained at birth. The IgM antibody titer in the infant's serum should be higher than the mother's titer, but they may be similar. For this reason, another sample from the infant at 1 month of age is tested simultaneously with the initial sample. The results should indicate a rise in IgM titer. Measurement of total IgM in the infant's sera at birth is nonspecific and may show false-negative and false-positive reactions.



Cytomegalovirus-infected human embryonic fibroblasts stained with fluorescein-labeled monoclonal antibody to early nuclear antigen (×1000).

60. The answer is c. *(Levinson, pp 190–191.)* Interferon is a protein that alters cell metabolism to inhibit viral replication. It induces the formation of a second protein that interferes with the translation of viral messenger RNA. Production of interferon has been demonstrated when cells in tissue culture are challenged with viruses, rickettsiae, endotoxin, or synthetic

double-stranded polynucleotides. Interferon confers species-specific, not virus-specific, protection for cells.

61. The answer is a. *(Murray, p 79.)* Viral cytopathic effects are thought to include a change in the host cell's macromolecular synthesis and the structure of the cell membrane. Viruses may produce cytopathic changes without forming infectious virions and without replicating infectious virus, although the cytopathology is usually fatal to the cell. A particular cytopathic effect is not necessarily associated with a specific virus.

62. The answer is a. *(Raoult, p 356.)* With an acute case of primary infection by Epstein-Barr virus (EBV), such as infectious mononucleosis, IgM antibodies to VCA should be present. Antibodies to EBNA should be absent, as they usually appear 2 to 3 months after onset of illness. Culture is not clinically useful because it (1) requires freshly fractionated cord blood lymphocytes, (2) takes 3 to 4 weeks for completion, and (3) is reactive in the majority of seropositive patients.

63. The answer is a. *(Raoult, pp 470–474.)* While the herpesviruses (HSV, CMV, VZV) are all well known for latency, adenovirus can also form a latent infection in the lymphoid tissue. In 50 to 80% of surgically removed tonsils or adenoids, adenovirus can be cultured. The virus has also been cultured from mesenteric lymph nodes, and, in rare cases, viral DNA has been detected in peripheral lymphocytes. Recurrent illness usually does not arise from these latent infections; however, activation can occur in the immunosuppressed.

64. The answer is e. *(Raoult, p 464.)* A therapeutic regimen that includes appropriately administered gamma globulin is effective in the treatment of viral hepatitis A and B. Hyperimmune rabies antiserum prolongs the incubation period of rabies and allows the patient more time to mount an immune response to the vaccine. Although it is not a primary form of treatment for patients with poliomyelitis, passive immunization with pooled gamma globulin can offer adequate protection against the disease.

65. The answer is b. *(Levinson, pp 214–215)* Atypical lymphocytes are the hematologic hallmark of infectious mononucleosis with 90% or more of the circulating lymphocytes being atypical in some cases. These abnor-

mal lymphocytes are not pathognomonic for infectious mononucleosis. They are also seen in other diseases, including cytomegalovirus infection, viral hepatitis, toxoplasmosis, rubella, mumps, and roseola.

66. The answer is a. *(Raoult, pp 284–285.)* Dengue (breakbone fever) is caused by a group B togavirus that is transmitted by mosquitoes. The clinical syndrome usually consists of a mild systemic disease characterized by severe joint and muscle pain, headache, fever, lymphadenopathy, and a maculopapular rash. Hemorrhagic dengue, a more severe syndrome, may be prominent during some epidemics; shock and occasionally death result.

67. The answer is b. *(Levinson, pp 248–249.)* HCV is a positive-stranded RNA virus, tentatively classified as a flavivirus. About half of HCV patients develop chronic hepatitis. A large number of infections appear among IV drug abusers. About 90% of the cases of transfusion-associated hepatitis are thought to be caused by HCV.

68–71. The answers are 68-b, 69-d, 70-a, 71-c. *(Levinson, pp 244–248.)* Advances in the serodiagnosis of viral hepatitis have been dramatic, and the findings of specific viral antigens have led to further elucidation of the course of infections. The "Australia antigen," discovered in 1960, was first renamed hepatitis-associated antigen (HAA) and then, finally, hepatitis B surface antigen (HBsAg). It appears in the blood early after infection, before onset of acute illness, and persists through early convalescence. HBsAg usually disappears within 4 to 6 months after the start of clinical illness except in the case of chronic carriers.

Hepatitis B 37 antigen (HBeAg) appears during the early acute phase and disappears before HBsAg is gone, although it may persist in the chronic carrier. Persons who are HBeAg-positive have higher titers of HBV and therefore are at a higher risk of transmitting the disease. HBeAg has a high correlation with DNA polymerase activity.

The hepatitis B core antigen (HBcAg) is found within the nuclei of infected hepatocytes and not generally in the peripheral circulation except as an integral component of the Dane particle. The antibody to this antigen, anti-HBc, is present at the beginning of clinical illness. As long as there is ongoing HBV replication, there will be high titers of anti-HBc. During the early convalescent phase of an HBV infection, anti-HBc may be the only detectable serologic marker (window phase) if HBsAg is negative and anti-HBsAg has not appeared.

72–76. The answers are 72-c, 73-e, 74-d, 75-a, 76-b. *(Levinson, pp 232–234, 239–240, 213–214, 229–230.)* The rabies virus is transmitted by the bite of a rabid animal. It almost always causes a fatal encephalitis if untreated. Postexposure treatment includes use of a killed vaccine and human rabies globulin (HIG). Rhinoviruses are the most prominent cause of the common cold. Many serotypes exist, which may account for their ability to cause frequent disease. Cytomegalovirus causes cytomegalic inclusion disease (CID), especially congenital abnormalities, in neonates. Malformations include microencephaly. Seizures, deafness, jaundice, and purpura can also occur. CID is also one of the leading causes of mental retardation in the United States. Respiratory syncytial virus (RSV) is the leading cause of pneumonia and bronchiolitis in infants. Viremia does not occur and treatment in several ill infants is aerosolized ribavirin. Orchitis, a complication of mumps virus infection in postpubertal males, can cause sterility if bilateral.

77–81. The answers are 77-b, 78-c, 79-d, 80-a, 81-e. *(Levinson, pp 197–198, 203–205.)* The original vaccine for hepatitis B was prepared by purifying hepatitis B surface antigen (HBsAg) from healthy HBsAg-positive carriers and treating it with viral-inactivating agents. The second-generation vaccine for hepatitis B is produced by recombinant DNA in yeast cells containing a plasmid into which the gene for HBsAg has been incorporated.

Influenza usually occurs in successive waves of infection with peak incidences during the winter months. If only minor antigenic drift is expected for the next influenza season, then the most recent strains of A and B viruses representative of the main antigens are included in the vaccine. Influenza vaccine consists of killed viruses.

Live attenuated measles virus vaccine effectively prevents measles. Protection is provided if given before or within 2 days of exposure. Vaccination confers immunity for at least 15 years.

Acyclovir is an analogue of guanosine or deoxyguanosine that strongly inhibits herpes simplex virus (HSV) but has little effect on other DNA viruses. When employed for the treatment of primary genital infection by HSV, both oral and intravenous formulations have reduced viral shedding and shortened the duration of symptoms.

The vaccine for hepatitis A virus (HAV) is prepared from virus grown in culture and inactivated with formalin. Passive immunization with immune serum globulin confers passive protection in 90% of those exposed when given within 1 to 2 weeks after exposure.

82–86. The answers are 82-c, 83-d, 84-e, 85-b, 86-a. *(Levinson, pp 212–213, 218–219, 219–220, 214–215.)* Varicella-zoster virus is a herpesvirus. Chickenpox is a highly contagious disease of childhood that occurs in the late winter and early spring. It is characterized by a generalized vesicular eruption with relatively insignificant systemic manifestations.

Adenovirus has been associated with adult respiratory disease among newly enlisted military troops. Crowded conditions and strenuous exercise may account for the severe infections seen in this otherwise healthy group.

Papillomavirus is one of two members of the family Papovaviridae, which includes viruses that produce human warts. These viruses are host-specific and produce benign epithelial tumors that vary in location and clinical appearance. The warts usually occur in children and young adults and are limited to the skin and mucous membranes.

Rotavirus is worldwide in distribution and has been implicated as the major etiologic agent of infantile gastroenteritis. Infection with this virus varies in its clinical presentation from asymptomatic infection to a relatively mild diarrhea to a severe and sometimes fatal dehydration. The exact mode of transmission of this infectious agent is not known. Because of severe side effects, the rotavirus vaccine has been recalled and is temporarily unavailable.

Infectious mononucleosis caused by cytomegalovirus (CMV) is clinically difficult to distinguish from that caused by Epstein-Barr virus. Lymphocytosis is usually present with an abundance of atypical lymphocytes. CMV-induced mononucleosis should be considered in any case of mononucleosis that is heterophil-negative and in patients with fever of unknown origin.

87–91. The answers are 87-c, 88-a, 89-c, 90-e, 91-b. *(Howard, pp 791–796.)* Epstein-Barr virus (EBV) is a herpesvirus that causes a number of syndromes; the most common is infectious mononucleosis. It is a ubiquitous enveloped DNA virus. Only one serotype of EBV has been recognized, although molecular methods have reorganized a number of genotypes of EBV.

Infectious mononucleosis is an acute disease most commonly seen in younger people. It is characterized by a proliferation of lymphocytes, lymph node enlargement, pharyngitis, fatigue, and fever. Infection in young children is usually either asymptomatic or characteristic of an acute upper respiratory infection. Diagnosis is usually made by a positive het-

erophil test. Heterophil antibodies are those that occur in one species (human) and react with antigens of a different species. The heterophil test may be insensitive (30 to 60%) in children. Definitive diagnosis is made by detection of antibodies to EBV components.

EBV causes a variety of other syndromes including Burkitt's lymphoma, the most common childhood cancer in Africa, and nasopharyngeal carcinoma, commonly seen in China.

Similar mononucleosis-like diseases are caused by cytomegalovirus (CMV) and *Toxoplasma gondii,* a parasite. CMV causes fewer than 10% of infectious mononucleosis-like diseases. CMV "mono" is primarily characterized by fatigue. Congenital infection with CMV almost always causes serious sequelae, such as retardation and hearing loss. *T. gondii* also causes a variety of clinical problems, among them encephalitis in AIDS patients and food poisoning from the ingestion of raw meat. Although CMV and *T. gondii* are relatively rare causes of infectious mononucleosis, they must be ruled out, particularly when EBV tests are nonreactive.

92–96. The answers are 92-a, 93-c, 94-e, 95-d, 96-d. *(Howard, pp 760–762.)* The diagnosis of a viral infection is made easier by the creation of a greater number of diagnostic virology laboratories during the past few decades. In order for viral diagnosis to be successful, the most appropriate specimen must be collected for the disease in question.

Human papillomavirus (HPV) is often detected microscopically in cervical biopsies. Alternatively, there are methods to detect HPV DNA in such tissues as well as to serotype the virus. Evidence suggests that some HPV serotypes are more likely than others to cause cervical cancer.

Many viruses have a viremic phase, but only a few, such as CMV, persist after the patient becomes symptomatic. CMV can be isolated from lymphocytes and polymorphonuclear leukocytes. This usually requires special separation procedures particularly in those compromised patients who may be neutropenic.

Enteroviruses such as echoviruses and coxsackieviruses are the predominant cause of aseptic viral meningitis. While enterovirus infections are often diagnosed by specific antibody response, it is possible to isolate the virus from CSF. Herpes simplex virus (HSV) can also be isolated from CSF in cases of herpes encephalitis or meningitis.

VZV and HSV are most often recovered from skin lesions, although varicella IgM antibody detection may be the most rapid way to diagnose

acute VZV infection. Detection and identification of these viruses is essential because of the availability of antiviral agents such as acyclovir. Other viruses, such as enteroviruses and paramyxoviruses, cause skin lesions.

Many viruses can be isolated from feces. Of the viral groups in these questions, adenovirus 40/41 is the most common stool isolate. Norwalk agent and other caliciviruses may also be isolated or detected from stools, but usually only in specialized laboratories.

97–101. The answers are 97-e, 98-b, 99-a, 100-c, 101-d. *(Howard, pp 833–836.)* A number of viruses that cause gastroenteritis are now being recognized. The table on page 51 summarizes the characteristics of rotavirus, Norwalk virus, adenovirus, calicivirus, and astrovirus.

102–106. The answers are 102-a, 103-c, 104-b, 105-e, 106-d. *(Levinson, pp 244–248.)* Hepatitis A virus (HAV) possesses a single-stranded linear RNA genome while hepatitis B virus (HBV) contains a double-stranded DNA genome. Detection of anti-HAV IgM in a single serum specimen obtained in the acute or convalescent stage is the quickest and most reliable method to diagnose hepatitis A infection. This antibody is usually present at onset of symptoms and may persist 3 to 6 months. Demonstration of hepatitis B surface antigen (HBsAg) in serum is the most common method of diagnosing HBV infection. Other serologic markers helpful in characterizing infection with HBV include hepatitis B surface antibody (anti-HBs), anti-hepatitis B core (anti-HBc), anti-hepatitis B e antigen (anti-HBe), and hepatitis B e antigen (HBeAg). Several epidemiologic studies have demonstrated that immune serum globulin (ISG) can prevent clinical hepatitis A even when given up to 10 days after exposure. Similar studies have shown that ISG was able to decrease the incidence of hepatitis B infection in exposed persons. Purified, noninfectious HBsAg derived from healthy HBsAg carriers has been used as a vaccine for active immunization for HBV infection. Hepatitis C is a single-stranded RNA virus belonging to the family Flaviviridae. The viral reservoir is human. Recent retrospective "lookbacks" suggest that many people were infected with HCV before testing of the blood supply was initiated in the early 1990s. HCV is treatable with combinations of drugs. The genotype of the virus plays an important role in the determination of length of therapy. Hepatitis D virus is an incomplete or defective virus which requires HBsAg as a cofactor. Both coinfection and secondary delta infection exist with secondary infection

	Norwalk and Norwalk-like Viruses	Rotavirus	Others		
			Adenovirus	Calicivirus	Astrovirus
Size (nm) diameter	27–35	70	70–90	35–39	
Nucleic acid	RNA (single-stranded)	RNA (double-stranded)	DNA	RNA	RNA
Minimum number of serotypes	3	4 (3 groups, A, B, C)	2	3–5	5
Seasonality (temperate climate)	Winter	Winter	All seasons	—	—
Epidemicity	Epidemic	Sporadic, epidemic	Sporadic	Epidemic	Sporadic
Age with clinical disease	≥6 yr	6–24 mo most common	≤2 yr	≤2 yr	≤7
Transmission	Fecal-oral, water, food	Fecal-oral, water, food	Fecal-oral	Fecal-oral	Fecal-oral

Source: Adapted from Howard BJ, Keiser JF, Smith TF, Weissfeld AS, Tilton RC: *Clinical and Pathogenic Microbiology,* 2/e, St. Louis, Mosby, 1993, with permission.

being the most serious. Hepatitis E virus is an RNA virus. Transmission is by the fecal-oral route although maternal-fetal transmission has recently been described. Prognosis is usually favorable with rare cases of fulminant HEV reported.

107–110. The answers are 107-a, 108-b, 109-b, 110-c. *(Levinson, pp 181, 220.)* Human papillomaviruses (HPV) are the causative agents of cutaneous warts as well as proliferative squamous lesions of mucosal surfaces. Although most infections by human papillomavirus are benign, some undergo malignant transformation into in situ and invasive squamous cell carcinoma. Both HPV and polyomavirus have icosahedral capsids and DNA genomes. JC virus, a polyomavirus, was first isolated from the diseased brain of a patient with Hodgkin's lymphoma who was dying of progressive multifocal leukoencephalopathy (PML). This demyelinating disease occurs usually in immunosuppressed persons and is the result of oligodendrocyte infection by JC virus. JC virus has also been isolated from the urine of patients suffering from demyelinating disease. Cryotherapy and laser treatment are the most popular therapies for warts, although surgery may be indicated in some cases. At the present time, there is no effective antiviral therapy for treatment of infection with polyomavirus or HPV. West Nile virus is an arbovirus. While prevalent in Europe, Africa, and the Middle East, it was not seen in the United States until the summer of 1999. It is transmitted by mosqitoes and birds, especially crows; these animals are a reservoir. WNV causes a rather mild encephalitis in humans, the exception being older patients or those who may be immunocompromised.

111–115. The answers are 111-b, 112-a, 113-c, 114-d, 115-e. *(Levinson, pp 222–226.)* Orthomyxoviruses and paramyxoviruses are RNA viruses that contain a single-stranded RNA genome. The influenza viruses belong to the orthomyxoviruses. They cause acute respiratory tract infections that usually occur in epidemics. Isolated strains of influenza virus are named after the virus type (influenza A, B, or C) as well as the host and location of initial isolation, the year of isolation, and the antigenic designation of the hemagglutinin and neuraminidase. Both the hemagglutinin and neuraminidase are glycoproteins under separate genetic control, and because of this they can and do vary independently. The changes in these antigens are responsible for the antigenic drift characteristic of these

viruses. The paramyxoviruses include several important human pathogens (mumps virus, measles virus, respiratory syncytial virus, and parainfluenza virus). Both paramyxoviruses and orthomyxoviruses possess an RNA-dependent RNA polymerase that is a structural component of the virion and produces the initial RNA. Respiratory syncytial viruses (RSV) are not related to the paramyxoviruses. They are 150-nm single-stranded RNA viruses. There are 2 antigen groups, A and B, which play no role in diagnosis and treatment. While the overall mortality is 0.5%, at-risk groups may be 25 to 35% mortality if untreated. Some parainfluenza virus infections (type 3) may be indistinguishable from RSV, but most parainfluenza infections produce a laryngotracheobronchitis known as croup.

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Bacteriology

Questions

DIRECTIONS: Each item below contains four or five suggested responses. Select the **one best** response to each question.

116. A patient with a peptic ulcer was admitted to the hospital and a gastric biopsy was performed. The tissue was cultured on chocolate agar incubated in a microaerophilic environment at 37°C for 5 to 7 days. At 5 days of incubation, colonies appeared on the plate and were curved, Gram-negative rods, oxidase-positive. The most likely identity of this organism is

a. *Campylobacter jejuni*
b. *Vibrio parahaemolyticus*
c. *Haemophilus influenzae*
d. *Helicobacter pylori*
e. *Campylobacter fetus*

117. An inhibitor was designed to block a biologic function in *H. influenzae*. If the goal of the experiment was to reduce the virulence of *H. influenzae,* the most likely target would be

a. Exotoxin liberator
b. Endotoxin assembly
c. Flagella synthesis
d. Capsule formation
e. IgA protease synthesis

118. An experimental compound is discovered that prevents the activation of adenyl cyclase and the resulting increase in cyclic AMP. The toxic effects of which of the following bacteria might be prevented with the use of this experimental compound?

a. *Vibrio cholerae*
b. *Corynebacterium diphtheriae*
c. *Pseudomonas*
d. *Listeria monocytogenes*
e. *Brucella*

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119. There are millions of cases of leprosy (Hansen's disease) worldwide, but predominately in Asia and Africa. The clinical spectrum of Hansen's disease is best characterized by

a. Immunologic anergy
b. Chronic pneumonitis
c. Peripheral neuritis
d. Bacilli in lesions that digest tissues
e. Erythematous lesions resembling concentric circles

Questions 120–121

120. At a church supper in Nova Scotia, the following meal was served: baked beans, ham, coleslaw, eclairs, and coffee. Of the 30 people who attended, 4 senior citizens became ill in 3 days; 1 eventually died. Two weeks after attending the church supper, a 19-year-old girl gave birth to a baby who rapidly became ill with meningitis and died in 5 days. Epidemiologic investigation revealed the following percentages of people who consumed the various food items: baked beans, 30%; ham, 80%; coleslaw, 60%; eclairs, 100%; and coffee, 90%. Which of the following statements is true?

a. This is not a case of food poisoning because only 4 people became ill
b. A relationship between the death of the baby and the food consumed at the church supper can be ruled out
c. Based on the epidemiologic investigation, the eclairs can be isolated as the source of the disease
d. Based on the epidemiologic investigation, the baked beans can be ruled out as the source of the disease
e. Additional epidemiologic data should include the percentage of those who ate a particular food item who became ill

121. Microbiologic analysis revealed no growth in the baked beans, ham, or coffee; many Gram-positive beta-hemolytic, short, rod-shaped bacteria in the coleslaw; and rare Gram-positive cocci in the eclairs. The most likely cause of this outbreak is

a. *Staphylococcus aureus*
b. *Listeria*
c. *Clostridium perfringens*
d. *Clostridium botulinum*
e. Nonmicrobiologic

Questions 122–124

A 21-year-old college student complained of malaise, low-grade fever, and a harsh cough, but not of muscle aches and pains. An x-ray revealed a diffuse interstitial pneumonia in the left lobes of the lung. The WBC count was normal. The student has been ill for a week.

122. Based on the information given, the most likely diagnosis is

a. Mycoplasma pneumonia
b. Pneumococcal pneumonia
c. Staphylococcal pneumonia
d. Influenza
e. Legionellosis

123. Based on the information given, which of the following laboratory tests would most rapidly assist you in making the diagnosis?

a. Cold agglutinins
b. Viral culture
c. Complement fixation (CF) test
d. Gram stain of sputum
e. Culture of sputum

124. The following laboratory data were available within 2 days: cold agglutinins—negative; complement fixation (*M. pneumoniae*)—1:64; viral culture—pending, but negative to date; bacterial culture of sputum on blood agar and MacConkey's agar—normal oral flora. In order to confirm the diagnosis, which of the following procedures could be ordered to achieve a specific and sensitive diagnosis?

a. Culture of the sputum on charcoal yeast extract
b. A repeat cold agglutinin test
c. A DNA probe to the 16S ribosomal RNA of an organism lacking a cell wall
d. A repeat CF test in 5 days
e. Another viral culture in 1 week

125. Pathogenic mechanisms involved in tuberculosis can be primarily attributed to which of the following?

a. Toxin production by the mycobacteria
b. Specific cell adhesion sites
c. Cell-mediated hypersensitivity
d. Humoral immunity
e. Clogging of alveoli by large numbers of acid-fast mycobacteria

126. The class of antibiotics known as the quinolones are bactericidal. Their mode of action on growing bacteria is thought to be

a. Inhibition of DNA gyrase
b. Inactivation of penicillin-binding protein II
c. Inhibition of β-lactamase
d. Prevention of the cross-linking of glycine
e. Inhibition of reverse transcriptase

127. Vancomycin-indeterminate *S. aureus* (VISA) has recently been reported in the United States. Which one of the statements concerning VISA is the most correct?

a. Minimum inhibitory concentration (MIC) for vancomycin is at least 1.0 mcg/mL
b. VISA isolates are usually methicillin susceptible (methicillin-resistant *S. aureus,* MRSA)
c. VISAs have emerged because of the extended use of vancomycin for MRSAs
d. Patients with VISA isolates need not be isolated
e. VISA isolates are infrequent, so surveillance at the present time is not warranted

128. A sputum sample was brought to the laboratory for analysis. Gram stain revealed the following: rare epithelial cells, 8 to 10 polymorphonuclear leukocytes per high-power field, and pleomorphic Gram-negative rods. As the laboratory consultant, which of the following interpretations should you make?

a. The sputum specimen is too contaminated by saliva to be useful
b. There is no evidence of an inflammatory response
c. The patient has pneumococcal pneumonia
d. The patient has Vincent's disease
e. The appearance of the sputum is suggestive of *Haemophilus pneumonia*

129. An isolate from a wound culture is a Gram-negative rod identified as *Bacteroides fragilis*. Anaerobic infection with *B. fragilis* is characterized by

a. A foul-smelling discharge
b. A black exudate in the wound
c. An exquisite susceptibility to penicillin
d. A heme-pigmented colony formation
e. Severe neurologic symptoms

130. Virtually all prokaryotic cells (bacteria, both Gram-positive and Gram-negative) contain peptidoglycan as well as specific enzymes for its synthesis. All of the following statements concerning Gram-positive and Gram-negative bacteria are true except

a. The extent of cross-linking of peptidoglycan is a function of different species of bacteria
b. The peptidoglycan-synthesizing enzymes can be antibiotic targets
c. Both Gram-positive and Gram-negative bacteria contain significant amounts of teichoic acid
d. With the exception of the structures that are cross-linked, peptidoglycan structure is common to most bacteria
e. The physical shape of bacteria is a function of peptidoglycan

131. *L. monocytogenes* causes a variety of diseases, including food poisoning. *Listeria* are small, Gram-positive, motile rod-shaped bacteria. Which of the following best describes these microorganisms?

a. *Listeria* are facultative intracellular pathogens
b. Once infected, the immune system cannot destroy *Listeria*
c. *Listeria* cannot be cultivated on artificial media
d. Flagella are produced both at room temperature and at 37°C
e. There is no relationship between *Listeria* serovars and human infection

132. A 30-year-old male patient was seen by the emergency service and reported a 2-week history of a penile ulcer. He noted that this ulcer did not hurt. Which one of the following conclusions/actions is most valid?

a. Draw blood for a herpes antibody test
b. Perform a dark-field examination of the lesion
c. Prescribe acyclovir for primary genital herpes
d. Even if treated, the lesion will remain for months
e. Failure to treat the patient will have no untoward effect, as this is a self-limiting infection

133. The laboratory reports that the Venereal Disease Research Laboratory (VDRL) test performed on the above patient is reactive at a dilution of 1:4 (4 dils). The patient also reports to you that he has recently been diagnosed with hepatitis A. Which one of the following actions would be most appropriate?

a. Report this patient to the health department, as he has syphilis
b. Order a confirmatory test such as the fluorescent treponemal antibody test (FTA)
c. Repeat the VDRL test
d. Order a rapid reagin test (RPR)
e. Perform a spinal tap to rule out central nervous system syphilis

134. In the above patient, which one of the following test combinations for syphilis is most appropriate?

a. FTA-Abs (IgG)/FTA-Abs (IgM)
b. RPR/FTA-Abs
c. RPR/culture of the lesion
d. VDRL/RPR
e. *Treponema pallidum* hemagglutination (TPHA)/microhemagglutination-*Treponema pallidum* (MHTP) tests

135. Assume that the patient absolutely denied any contact, sexual or otherwise, with a person who had syphilis. Assume also that both the RPR and the FTA Abs were positive on this patient. Which one of the following tests could be used to show that this patient probably does not have syphilis?

a. VDRL
b. Quantitative RPR
c. *Treponema pallidum* immobilization (TPI) test
d. Frei test
e. MHTP test

136. A 55-year-old man who is being treated for adenocarcinoma of the lung is admitted to a hospital because of a temperature of 38.9°C (102°F), chest pain, and a dry cough. Sputum is collected. Gram's stain of the sputum is unremarkable and culture reveals many small Gram-negative rods able to grow only on a charcoal yeast extract agar. This organism most likely is

a. *Klebsiella pneumoniae*
b. *Mycoplasma pneumoniae*
c. *Legionella pneumophila*
d. *Chlamydia trachomatis*
e. *S. aureus*

137. A patient was hospitalized after an automobile accident. The wounds became infected and the patient was treated with tobramycin, carbenicillin, and clindamycin. Five days after antibiotic therapy was initiated, the patient developed severe diarrhea and pseudomembranous enterocolitis. Antibiotic-associated diarrhea and the more serious pseudomembranous enterocolitis can be caused by

a. *Clostridium sordellii*
b. *Clostridium perfringens*
c. *Clostridium difficile*
d. *S. aureus*
e. *B. fragilis*

138. Assuming that the average achievable serum level of gentamicin is 6 to 8 mcg/mL, which of the following bacteria is susceptible to gentamicin?

a. *E. coli* with a minimal inhibitory concentration (MIC) of 10 mcg/mL
b. *E. coli* with an MIC of 12 mcg/mL
c. *Klebsiella* with an MIC of 0.25 mcg/mL
d. *Klebsiella* with an MIC of 6.0 mcg/mL
e. *Klebsiella* with an MIC of 20 mcg/mL

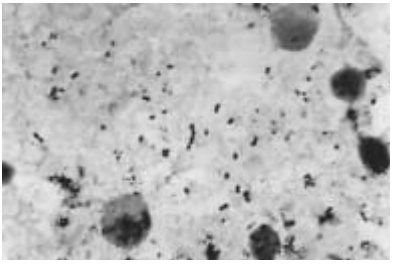
139. A child comes to an emergency room because of an infected dog bite. The wound is found to contain small Gram-negative rods. The most likely cause of infection is

a. *E. coli*
b. *H. influenzae*
c. *Pasteurella multocida*
d. *Brucella canis*
e. *Klebsiella rhinoscleromatis*

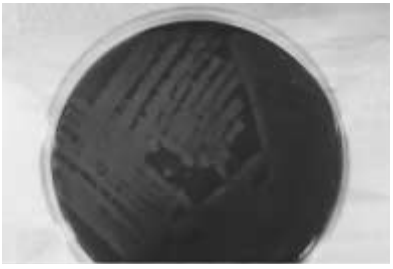
140. A patient complained to his dentist about a draining lesion in his mouth. A Gram's stain of the pus showed a few Gram-positive cocci, leukocytes, and many branched Gram-positive rods. The most likely cause of the disease is

a. *Actinomyces israelii*
b. *Actinomyces viscosus*
c. *C. diphtheriae*
d. *Propionibacterium acnes*
e. *S. aureus*

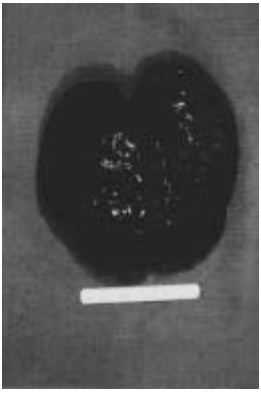
141. A female infant was born prematurely after rupture of membranes and, within 1 day of birth, developed a fever and died. The pregnant mother had been cultured just prior to the birth of her child and her vaginal culture revealed group B streptococci (*S. agalactiae*). Which one of the pictured tests shown in the figure below would provide the most rapid and useful information?



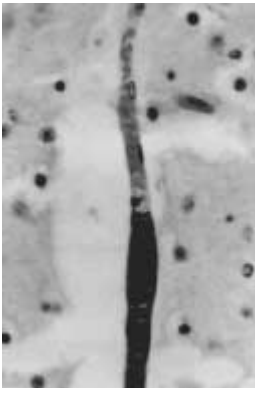
A.



B.



C.



D.

A. Direct Gram stain demonstrating *Streptococcus agalactiae* in CSF of infected neonate (μ1000). **B.** Blood agar plate demonstrating diffuse β-hemolysis due to group B streptococci from CSF. **C.** Brain at autopsy demonstrating acute hemorrhagic response to *Streptococcus agalactiae*. **D.** Brain section with blood vessel occluded by group B streptococci.

142. Group B streptococcus sepsis in an infant is preventable. Which one of the following procedures is most likely to reduce the incidence of group B streptococcal disease?

a. Intrapartum antibiotic treatment
b. Use of a polysaccharide vaccine
c. Screening of pregnant females in the last trimester
d. Identification of possible high-risk births
e. Screening of pregnant females at the first office visit, usually during the first trimester

143. There has been much speculation on the pathogenesis of group B streptococcal disease in the neonate. One of the most likely pathogenic mechanisms is

a. Complement C5a, a potent chemoattractant, activates PMNs
b. The streptococci are resistant to penicillin
c. The alternative complement pathway is activated
d. In the absence of specific antibody, opsonization, phagocyte recognition, and killing do not proceed normally

144. A man who has a penile chancre appears in a hospital's emergency service. The VDRL test is negative. The most appropriate course of action for the physician in charge would be to

a. Send the patient home untreated
b. Repeat the VDRL test in 10 days
c. Perform dark-field microscopy for treponemes
d. Swab the chancre and culture on Thayer-Martin agar
e. Perform a Gram stain on the chancre fluid

145. Fever of unknown origin in a farmer who raises goats would most likely be caused by which of the following organisms?

a. *Brucella melitensis*
b. *Clostridium novyi*
c. *T. pallidum*
d. *Histoplasma capsulatum*
e. *Mycobacterium tuberculosis*

146. Cholera is a toxicogenic dysenteric disease common in many parts of the world. In the treatment of patients who have cholera, the use of a drug that inhibits adenyl cyclase would be expected to

a. Kill the patient immediately
b. Eradicate the organism
c. Increase fluid secretion
d. Reduce intestinal motility
e. Block the action of cholera toxin

147. A box of ham sandwiches with mayonnaise prepared by a person with a boil on his neck was left out of the refrigerator for the on-call interns. Three doctors became violently ill approximately 2 h after eating the sandwiches. The most likely cause is

a. *S. aureus* enterotoxin
b. Coagulase from *S. aureus* in the ham
c. *S. aureus* leukocidin
d. *C. perfringens* toxin
e. Penicillinase given to inactivate penicillin in the pork

148. *S. aureus* causes a wide variety of infections, ranging from wound infection to pneumonia. Treatment of *S. aureus* infection with penicillin is often complicated by the

a. Inability of penicillin to penetrate the membrane of *S. aureus*
b. Production of penicillinase by *S. aureus*
c. Production of penicillin acetylase by *S. aureus*
d. Lack of penicillin binding sites on *S. aureus*
e. Allergic reaction caused by staphylococcal protein

149. Symptoms of *C. botulinum* food poisoning include double vision, inability to speak, and respiratory paralysis. These symptoms are consistent with

a. Invasion of the gut epithelium by *C. botulinum*
b. Secretion of an enterotoxin
c. Endotoxin shock
d. Ingestion of a neurotoxin
e. Activation of cyclic AMP

150. In people who have sickle cell anemia, osteomyelitis usually is associated with which of the following organisms?

a. *Micrococcus*
b. *Escherichia*
c. *Pseudomonas*
d. *Salmonella*
e. *Streptococcus*

151. The treatment of choice for a patient with *C. jejuni* enterocolitis is

a. Erythromycin
b. Ciprofloxacin
c. Ampicillin
d. Pepto-Bismol
e. *Campylobacter* antitoxin

152. A hyperemic edema of the larynx and epiglottis that rapidly leads to respiratory obstruction in young children is most likely to be caused by

a. *K. pneumoniae*
b. *M. pneumoniae*
c. *Neisseria meningitidis*
d. *H. influenzae*
e. *H. hemolyticus*

Questions 153–154

A 70-year-old female patient was readmitted to a local hospital with fever and chills following cardiac surgery at a major teaching institution. Blood cultures were taken and a Gram-positive coccus grew from the blood cultures within 24 hours. Initial tests indicated that this isolate was resistant to penicillin.

153. The most likely identification is

a. *Streptococcus pneumoniae*
b. *Neisseria*
c. Group A streptococcus
d. Enterococcus
e. Group B streptococcus

154. Further testing revealed that the isolate possessed the group D antigen, was not β-lactamase-positive, but was resistant to vancomycin. The most likely identification of this isolate is

a. *Enterococcus faecalis*
b. *Enterococcus durans*
c. *Enterococcus cassiflavus*
d. *S. pneumoniae*
e. *Enterococcus faecium*

155. The treatment of choice for the isolate in question 153 is

a. Gentamicin
b. Gentamicin and ampicillin
c. Ciprofloxacin
d. Rifampin
e. No available treatment

156. Acute hematogenous osteomyelitis is often diagnosed by isolation of the organism from the blood and is caused most often by

a. *Proteus mirabilis*
b. *Streptococcus faecalis*
c. *Staphylococcus epidermidis*
d. *S. aureus*
e. *E. coli*

157. Diphtheria toxin is produced only by those strains of *C. diphtheriae* that are

a. Glucose fermenters
b. Sucrose fermenters
c. Lysogenic for β-prophage
d. Of the mitis strain
e. Encapsulated

Questions 158–160

A 28-year-old menstruating woman appeared in the emergency room with the following signs and symptoms: fever, 104°F (40°C); WBC, 16,000/μL; blood pressure, 90/65 mmHg; a scarlatiniform rash on her trunk, palms, and soles; extreme fatigue; vomiting; and diarrhea.

158. The patient described in the case above most likely has

a. Scalded skin syndrome
b. Toxic shock syndrome
c. Guillain-Barré syndrome
d. Chickenpox
e. Staphylococcal food poisoning

159. Culture of the menstrual fluid in the case cited would most likely reveal a predominance of

a. *S. aureus*
b. *S. epidermidis*
c. *C. perfringens*
d. *C. difficile*
e. *Gardnerella vaginalis*

160. The most characteristic finding not yet revealed in the case just presented would be

a. Travel to Vermont
b. Recent exposure to rubella
c. A retained tampon
d. Heavy menstrual flow
e. A meal of chicken in a fast-food restaurant

Questions 161–164

A new latex agglutination (LA) reagent for *H. influenzae* polysaccharide antigen in cerebrospinal fluid was evaluated. Results were compared with the isolation of *H. influenzae* from the CSF. Results were as follows:

LA POS, CULT POS: 25
LA POS, CULT NEG: 5
LA NEG, CULT POS: 5
LA NEG, CULT NEG: 95

161. The sensitivity of LA is

a. 0%
b. 30%
c. 85%
d. 95%
e. 100%

162. The specificity of LA is

a. 0%
b. 30%
c. 80%
d. 95%
e. 100%

163. The negative predictive value of LA is

a. 10%
b. 80%
c. 95%
d. 110%
e. Not calculable

164. The incidence of *H. influenzae* meningitis in the general population is less than 1%. If during an epidemic the incidence rose to 3%, the negative predictive value of the LA test would

a. Increase
b. Decrease
c. Remain the same
d. Be impossible to calculate
e. Vary as a function of the specificity of the LA test

165. Methicillin-resistant *S. aureus* (MRSA) was isolated from 7 patients in a 14-bed intensive care unit. All patients were isolated and the unit closed to any more admissions. Which one of the following reasons best explains these rigorous methods to control MRSA?

a. MRSA is inherently more virulent than other staphylococci
b. The alternative for treatment of MRSA is vancomycin, an expensive and potentially toxic antibiotic
c. MRSA causes toxic shock syndrome
d. MRSA spreads more rapidly from patient to patient than antibiotic-susceptible staphylococci do
e. MRSA is resistant to penicillin

166. A patient with AIDS returned from Haiti with acute diarrhea. The stool revealed an oval organism (8 to 9 μm in diameter) that was acid-fast and fluoresced blue under ultraviolet light. The most likely identification of this organism is

a. *Cyclospora*
b. *Giardia*
c. *Enterocytozoon*
d. *Cryptosporidium*
e. *Prototheca*

167. A 2-year-old infant is brought to the emergency room with hemolytic uremic syndrome and thrombocytopenia. Which one of the following bacteria would most likely be isolated from a stool specimen?

a. *Shigella*
b. *Salmonella*
c. *Aeromonas*
d. *E. coli* 0157/H7
e. *Enterobacter*

168. *E. coli* causes disease by a variety of different methods. Which one of the following *E. coli* types is characterized by the presence of LT (heat-labile) and ST (heat-stable) proteins?

a. Enteroinvasive (EIEC)
b. Enterotoxigenic (ETEC)
c. Enterohemorrhagic (EHEC)
d. Enteropathogenic (EPEC)
e. Enterohemolytic (EHEEC)

169. *Yersinia pestis,* the causative agent of plague, is enzootic in the United States west of the one-hundredth meridian. Human plague can be bubonic or pneumonic. The primary epidemiologic difference between the two clinical forms of plague is

a. Season of the year
b. Route of infection
c. Age of the patient
d. Health of the animal vector
e. Geographic location of the animal vector

170. A 9-year-old child is brought to the emergency room with the chief complaint of enlarged, painful axillary lymph nodes. The resident physician also notes a small, inflamed, dime-sized lesion surrounding what appears to be a small scratch on the forearm. The lymph node is aspirated and some pus is sent to the laboratory for examination. A Warthin-Starry silver impregnation stain reveals many highly pleomorphic, rod-shaped bacteria. The most likely cause of this infection is

a. *Y. pestis*
b. *Yersinia enterocolitica*
c. *Mycobacterium scrofulaceum*
d. *B. canis*
e. *Bartonella henselae*

171. Recently, there have been sensational media reports of patients infected with invasive, "flesh-eating" bacteria that spread rapidly through the tissues. This necrotizing fasciitis is usually caused by

a. *S. aureus*
b. Group A streptococci
c. *Micrococcus*
d. *Bacillus cereus*
e. *Clostridium tetani*

172. The most effective noninvasive test for the diagnosis of *Helicobacter*-associated gastric ulcers is

a. Detection of *H. pylori* antigen in stool
b. Growth of *H. pylori* from a stomach biopsy
c. Growth of *H. pylori* in the stool
d. IgM antibodies to *H. pylori*
e. Culture of stomach contents for *H. pylori*

173. The following test results were observed in a woman tested in November who reported being in the woods in Pennsylvania during the past summer, was bitten by a tick, and now has Bell's palsy: Lyme IgG antibody 1:1280; Lyme IgM antibody negative. Which one of the following courses of action is most appropriate?

a. Order tests for syphilis (VDRL, FTA-ABS) because there are cross-reactions reported with *Borrelia burgdorferi*
b. Ask the patient if she has a severe headache
c. Consider treatment of the patient with an appropriate antibiotic such as tetracycline
d. Ask the patient if she has had a urinary tract infection with *E. coli*
e. Ignore the results because there is no Lyme disease in Pennsylvania

174. *Mycobacterium avium* is a major opportunistic pathogen in AIDS patients. *M. avium* from AIDS patients can be best characterized by which one of the following statements?

a. The majority of *M. avium* isolates from AIDS patients are nonpigmented
b. *M. avium* isolates from AIDS patients are of multiple serovars
c. Few isolates from AIDS patients are acid-fast
d. Most isolates from AIDS patients are sensitive to isoniazid and streptomycin
e. *M. avium* can be isolated from the blood of AIDS patients

175. Rheumatic fever (RF) is a disease seen in children and young adults. Which one of the following statements best typifies the disease?

a. It is characterized by inflammatory lesions that may involve the heart, joints, subcutaneous tissues, and the central nervous system
b. The pathogenesis is related to the similarity between a staphylococcal antigen and a human cardiac antigen
c. Prophylaxis with benzathine penicillin is of little value
d. It is a complication of group A streptococcal skin disease but usually not of pharyngitis
e. It is very common in developing countries but extremely rare and decreasing in incidence in the United States

176. The fermentation patterns for four strains of Gram-negative cocci are given below (strains C and D grow on plain nutrient agar). Which of these strains is likely to cause venereal disease in humans?

	Acid Produced From		
	Maltose	**Dextrose**	**Sucrose**
a. Strain A	+	+	−
b. Strain B	−	+	−
c. Strain C	−	−	−
d. Strain D	+	+	+

177. If a quellung test was done on the following bacterial isolates, which one would you expect to be positive?

a. *S. pneumoniae*
b. *Enterobacter*
c. *Haemophilus parainfluenzae*
d. *C. diphtheriae*
e. *N. gonorrhoeae*

178. Bacteria cause disease in a number of ways. One mechanism of pathogenesis is the secretion of potent protein toxins. All the following diseases are caused by microbial protein toxins, but one toxin has been used for a variety of maladies. It is

a. Tetanus
b. Botulism
c. Bacillary (*Shigella*) dysentery
d. Diphtheria
e. Disseminated intravascular coagulation

179. A 2-year-old child was admitted to the hospital with acute meningitis. The Gram stain revealed Gram-positive short rods, and the mother indicated that the child had received "all" of the meningitis vaccinations. What is the most likely cause of the disease?

a. *N. meningitidis,* group A
b. *N. meningitidis,* group C
c. *Listeria*
d. *S. pneumoniae*
e. *H. influenzae*

180. The most common portal of entry for *C. tetani,* the cause of tetanus, is the

a. Skin
b. Gastrointestinal tract
c. Respiratory tract
d. Genital tract
e. Nasal tract

181. The most common way in which tuberculosis is acquired is via the

a. Skin
b. Gastrointestinal tract
c. Respiratory tract
d. Genital tract
e. Nasal tract

182. Shigellosis is common in travelers to developing countries. Infection is commonly acquired through the

a. Skin
b. Gastrointestinal tract
c. Respiratory tract
d. Genital tract
e. Nasal tract

183. A person who contracts gonorrhea is most likely to have acquired it via the

a. Skin
b. Gastrointestinal tract
c. Respiratory tract
d. Genital tract
e. Nasal tract

184. There are a variety of "unusual" bacteria that infect humans. While rare, disease caused by these microorganisms is serious and occasionally difficult to identify. *Branhamella* is best characterized as

a. A Gram-negative pleomorphic rod that can cause endocarditis
b. The causative agent of trench fever
c. A Gram-negative rod, fusiforme-shaped, that is associated with periodontal disease but may cause sepsis
d. The causative agent of rat-bite fever
e. The causative agent of sinusitis, bronchitis, and pneumonia

185. *Cardiobacterium* is best characterized as

a. A Gram-negative pleomorphic rod that can cause endocarditis
b. The causative agent of trench fever
c. A Gram-negative rod, fusiforme-shaped, that is associated with periodontal disease but may cause sepsis
d. The causative agent of rat-bite fever
e. The causative agent of sinusitis, bronchitis, and pneumonia

186. *Capnocytophyga* is best characterized as

a. A Gram-negative pleomorphic rod that can cause endocarditis
b. The causative agent of trench fever
c. A Gram-negative rod, fusiforme-shaped, that is associated with periodontal disease but may cause sepsis
d. The causative agent of rat-bite fever
e. The causative agent of sinusitis, bronchitis, and pneumonia

187. An enterococcus (*E. faecium*) was isolated from a urine specimen (100,000 cfu/mL). Treatment of the patient with ampicillin and gentamicin failed. The most clinically appropriate action is

a. Do no further clinical workup
b. Suggest to the laboratory that low colony counts may reflect infection
c. Determine if fluorescent microscopy is available for the diagnosis of actinomycosis
d. Consider vancomycin as an alternative drug
e. Suggest a repeat antibiotic susceptibility test

188. A patient with symptoms of urinary tract infection had a culture taken, which grew 5×10^3 *E. coli*. The laboratory reported it as "insignificant." The most clinically appropriate action is

a. Do no further clinical workup
b. Suggest to the laboratory that low colony counts may reflect infection
c. Determine if fluorescent microscopy is available for the diagnosis of actinomycosis
d. Consider vancomycin as an alternative drug
e. Suggest a repeat antibiotic susceptibility test

189. A patient appeared in the emergency room with a submandibular mass. A smear was made of the drainage and a bewildering variety of bacteria were seen, including branched, Gram-positive rods. The most clinically appropriate action is

a. Do no further clinical workup
b. Suggest to the laboratory that low colony counts may reflect infection
c. Determine if fluorescent microscopy is available for the diagnosis of actinomycosis
d. Consider vancomycin as an alternative drug
e. Suggest a repeat antibiotic susceptibility test

190. The antibiotic therapy of choice for legionellosis is

a. Penicillin
b. Ampicillin
c. Erythromycin
d. Vancomycin
e. Ceftriaxone

191. The antibiotic of choice for pneumococcal pneumonia is

a. Penicillin
b. Ampicillin
c. Erythromycin
d. Vancomycin
e. Ceftriaxone

192. The antibiotic of choice for Lyme disease is

a. Penicillin
b. Ampicillin
c. Erythromycin
d. Vancomycin
e. Ceftriaxone

193. The antibiotic of choice for streptococcal pharyngitis is

a. Penicillin
b. Ampicillin
c. Erythromycin
d. Vancomycin
e. Ceftriaxone

194. The therapy of choice for pseudomembranous enterocolitis is

a. Penicillin
b. Ampicillin
c. Erythromycin
d. Vancomycin
e. Ceftriaxone

Questions 195–198

Although cholera, a *Vibrio* infection, has been rarely seen in the United States, there have been recent outbreaks of classic cholera associated with shellfish harvested from the Gulf of Mexico. Vibrios are shaped like curved rods, and infections more common than cholera may be caused by a variety of curved-rod bacteria.

195. *C. jejuni* is best described as

a. "String-test"-positive isolate; three serotypes—Ogawa (AB), Inaba (AC), Hikojima (ABC)
b. Human pathogen, halophilic, lactose-positive; produces heat-labile, extracellular toxin
c. Human pathogen, halophilic, lactose-negative, sucrose-negative; causes gastrointestinal diseases primarily from ingestion of cooked seafood
d. Cause of gastroenteritis; reservoir in birds and mammals, optimal growth at 42°C
e. Urease-positive; cause of fetal distress in cattle

196. *V. cholerae,* the causative agent of cholera, is best described as

a. "String-test"-positive isolate; three serotypes—Ogawa (AB), Inaba (AC), Hikojima (ABC)
b. Human pathogen, halophilic, lactose-positive; produces heat-labile, extracellular toxin
c. Human pathogen, halophilic, lactose-negative, sucrose-negative; causes gastrointestinal diseases primarily from ingestion of cooked seafood
d. Cause of gastroenteritis; reservoir in birds and mammals, optimal growth at 42°C
e. Urease-positive; cause of fetal distress in cattle

197. *V. parahaemolyticus,* first described in Japan, is best characterized as

a. "String-test"-positive isolate; three serotypes—Ogawa (AB), Inaba (AC), Hikojima (ABC)
b. Human pathogen, halophilic, lactose-positive; produces heat-labile, extracellular toxin
c. Human pathogen, halophilic, lactose-negative, sucrose-negative; causes gastrointestinal diseases primarily from ingestion of cooked seafood
d. Cause of gastroenteritis; reservoir in birds and mammals, optimal growth at 42°C
e. Urease-positive; cause of fetal distress in cattle

198. *Vibrio vulnificus,* which can be found in the oceans and bays in temperate and tropical climates, is best characterized as

a. "String-test"-positive isolate; three serotypes—Ogawa (AB), Inaba (AC), Hikojima (ABC)
b. Human pathogen, halophilic, lactose-positive; produces heat-labile, extracellular toxin
c. Human pathogen, halophilic, lactose-negative, sucrose-negative; causes gastrointestinal diseases primarily from ingestion of cooked seafood
d. Cause of gastroenteritis; reservoir in birds and mammals, optimal growth at 42°C
e. Urease-positive; cause of fetal distress in cattle

Questions 199–202

Each bacterium listed below is a small, Gram-negative rod. Some of them are fastidious and may be difficult to culture and identify. They have unique microbiological features and each of them causes distinctive clinical disease.

199. *Y. enterocolitica,* formerly a *Pasteurella,* is best described by which of the following statements?

a. Commonly inhabits the canine respiratory tract and is an occasional pathogen for humans; strongly urease-positive
b. Pits agar, grows both in carbon dioxide and under anaerobic conditions, and is part of the normal oral cavity flora
c. Typically infects cattle, requires 5 to 10% carbon dioxide for growth, and is inhibited by the dye thionine
d. Typically is found in infected animal bites in humans and can cause hemorrhagic septicemia in animals
e. Manifests different biochemical and physiologic characteristics, depending on growth temperature, and causes a spectrum of human disease, most commonly mesenteric lymphadenitis

200. *Brucella abortus,* one of the three species causing brucellosis, a possible bioterrorism agent, is best described by which of the following statements?

a. Commonly inhabits the canine respiratory tract and is an occasional pathogen for humans; strongly urease-positive
b. Pits agar, grows both in carbon dioxide and under anaerobic conditions, and is part of the normal oral cavity flora
c. Typically infects cattle, requires 5 to 10% carbon dioxide for growth, and is inhibited by the dye thionine
d. Typically is found in infected animal bites in humans and can cause hemorrhagic septicemia in animals
e. Manifests different biochemical and physiologic characteristics, depending on growth temperature, and causes a spectrum of human disease, most commonly mesenteric lymphadenitis

201. *Bordetella bronchiseptica* could be confused with the agent of whooping cough. It is best described by which of the following statements?

a. Commonly inhabits the canine respiratory tract and is an occasional pathogen for humans; strongly urease-positive
b. Pits agar, grows both in carbon dioxide and under anaerobic conditions, and is part of the normal oral cavity flora
c. Typically infects cattle, requires 5 to 10% carbon dioxide for growth, and is inhibited by the dye thionine
d. Typically is found in infected animal bites in humans and can cause hemorrhagic septicemia in animals
e. Manifests different biochemical and physiologic characteristics, depending on growth temperature, and causes a spectrum of human disease, most commonly mesenteric lymphadenitis

202. *P. multocida* is a very common organism and is best described by which of the following statements?

a. Commonly inhabits the canine respiratory tract and is an occasional pathogen for humans; strongly urease-positive
b. Pits agar, grows both in carbon dioxide and under anaerobic conditions, and is part of the normal oral cavity flora
c. Typically infects cattle, requires 5 to 10% carbon dioxide for growth, and is inhibited by the dye thionine
d. Typically is found in infected animal bites in humans and can cause hemorrhagic septicemia in animals
e. Manifests different biochemical and physiologic characteristics, depending on growth temperature, and causes a spectrum of human disease, most commonly mesenteric lymphadenitis

Questions 203–207

To isolate specific bacteria from clinical specimens, it is necessary to use a variety of artificial media, some of which is selective, others of which are nonselective.

203. *N. gonorrhoeae* is a fastidious pathogen and found in sites often contaminated with normal flora. The best medium for isolation is

a. Sheep blood agar
b. Löffler's medium
c. Thayer-Martin agar
d. Thiosulfate citrate bile salts sucrose medium
e. Löwenstein-Jensen medium

204. *V. cholerae,* the causative agent of cholera, is best isolated using

a. Sheep blood agar
b. Löffler's medium
c. Thayer-Martin agar
d. Thiosulfate citrate bile salts sucrose medium
e. Löwenstein-Jensen medium

205. *M. tuberculosis* can be found in the sputum of patients with tuberculosis. After digestion of the sputum, isolation is best accomplished using

a. Sheep blood agar
b. Löffler's medium
c. Thayer-Martin agar
d. Thiosulfate citrate bile salts sucrose medium
e. Löwenstein-Jensen medium

206. *C. diphtheriae* may be difficult to isolate from the nasopharynx without the use of special media. The medium of choice is

a. Sheep blood agar
b. Löffler's medium
c. Thayer-Martin agar
d. Thiosulfate citrate bile salts sucrose medium
e. Löwenstein-Jensen medium

207. *S. aureus* has a distinctive appearance on which one of the following media?

a. Sheep blood agar
b. Löffler's medium
c. Thayer-Martin agar
d. Thiosulfate citrate bile salts sucrose medium
e. Löwenstein-Jensen medium

Questions 208–211

In order to recognize abnormal bacteria, it is necessary to know which bacteria are predominant normal flora of certain body sites.

208. Which of the following is the predominant organism on skin commonly seen as a blood culture contaminant?

a. α-hemolytic streptococci
b. *Lactobacillus*
c. *S. epidermidis*
d. *Escherichia coli*
e. *B. fragilis*

209. Which of the following is the predominant flora of the mouth that is the major cause of dental caries?

a. α-hemolytic streptococci
b. *Lactobacillus*
c. *S. epidermidis*
d. *E. coli*
e. *B. fragilis*

210. The bowel contains many microorganisms but the most prevalent bacterium is

a. α-hemolytic streptococci
b. *Lactobacillus*
c. *S. epidermidis*
d. *E. coli*
e. *B. fragilis*

211. Which of the following is the most prevalent microorganism in the vagina that may also be protective?

a. α-hemolytic streptococci
b. *Lactobacillus*
c. *S. epidermidis*
d. *E. coli*
e. *B. fragilis*

212. *Streptococcus mutans* is best described as

a. A facultative anaerobe that often inhabits the buccal mucosa early in a neonate's life and can cause bacterial endocarditis
b. A β-hemolytic organism that causes a diffuse, rapidly spreading cellulitis
c. An anaerobic, filamentous bacterium that often causes cervicofacial osteomyelitis
d. A facultative anaerobe that is highly cariogenic and sticks to teeth by synthesis of a dextran
e. A facultatively anaerobic, rod-shaped bacterium that sticks to teeth and is cariogenic

213. *Streptococcus salivarius,* a common isolate in the clinical laboratory, is best described as

a. A facultative anaerobe that often inhabits the buccal mucosa early in a neonate's life and can cause bacterial endocarditis
b. A β-hemolytic organism that causes a diffuse, rapidly spreading cellulitis
c. An anaerobic, filamentous bacterium that often causes cervicofacial osteomyelitis
d. A facultative anaerobe that is highly cariogenic and sticks to teeth by synthesis of a dextran
e. A facultatively anaerobic, rod-shaped bacterium that sticks to teeth and is cariogenic

214. *A. israelii* is one of many actinomycetes and is best described as

a. A facultative anaerobe that often inhabits the buccal mucosa early in a neonate's life and can cause bacterial endocarditis
b. A β-hemolytic organism that causes a diffuse, rapidly spreading cellulitis
c. An anaerobic, filamentous bacterium that often causes cervicofacial osteomyelitis
d. A facultative anaerobe that is highly cariogenic and sticks to teeth by synthesis of a dextran
e. A facultatively anaerobic, rod-shaped bacterium that sticks to teeth and is cariogenic

215. *A. viscosus,* another ubiquitous actinomycete, can best be described as

a. A facultative anaerobe that often inhabits the buccal mucosa early in a neonate's life and can cause bacterial endocarditis
b. A β-hemolytic organism that causes a diffuse, rapidly spreading cellulitis
c. An anaerobic, filamentous bacterium that often causes cervicofacial osteomyelitis
d. A facultative anaerobe that is highly cariogenic and sticks to teeth by synthesis of a dextran
e. A facultatively anaerobic, rod-shaped bacterium that sticks to teeth and is cariogenic

216. *C. diphtheriae* causes diphtheria, a rare disease in the United States. *C. diphtheriae* is best characterized by which of the following statements?

a. It secretes erythrogenic toxin that causes the characteristic signs of scarlet fever
b. It produces toxin that blocks protein synthesis in an infected cell and carries a lytic bacteriophage that produces the genetic information for toxin production
c. It produces at least one protein toxin consisting of two subunits, A and B, that cause severe spasmodic cough usually in children
d. It requires cysteine for growth
e. It secretes exotoxin that has been called "verotoxin" and "Shiga-like toxin"; infection is mediated by specific attachment to mucosal membranes

217. *Bordetella pertussis* is a Gram-negative rod that causes severe respiratory disease. Which one of the following statements best characterizes this microorganism?

a. It secretes erythrogenic toxin that causes the characteristic signs of scarlet fever
b. It produces toxin that blocks protein synthesis in an infected cell and carries a lytic bacteriophage that produces the genetic information for toxin production
c. It produces at least one protein toxin consisting of two subunits, A and B, that cause severe spasmodic cough usually in children
d. It requires cysteine for growth
e. It secretes exotoxin that has been called "verotoxin" and "Shiga-like toxin"; infection is mediated by specific attachment to mucosal membranes

218. *Francisella tularensis* is the bacterium that causes tularemia, a disease not uncommonly seen in hunters. Which one of the following statements best characterizes this bacterium?

a. It secretes erythrogenic toxin that causes the characteristic signs of scarlet fever
b. It produces toxin that blocks protein synthesis in an infected cell and carries a lytic bacteriophage that produces the genetic information for toxin production
c. It produces at least one protein toxin consisting of two subunits, A and B, that cause severe spasmodic cough usually in children
d. It requires cysteine for growth
e. It secretes exotoxin that has been called "verotoxin" and "Shiga-like toxin"; infection is mediated by specific attachment to mucosal membranes

219. *E. coli* 0157/H7 is a newsworthy microorganism that has been isolated from foods (meat) and beverages (cider) with increasing frequency. Its characteristic biology is best described by which of the following statements?

a. It secretes erythrogenic toxin that causes the characteristic signs of scarlet fever
b. It produces toxin that blocks protein synthesis in an infected cell and carries a lytic bacteriophage that produces the genetic information for toxin production
c. It produces at least one protein toxin consisting of two subunits, A and B, that cause severe spasmodic cough usually in children
d. It requires cysteine for growth
e. It secretes exotoxin that has been called "verotoxin" and "Shiga-like toxin"; infection is mediated by specific attachment to mucosal membranes

220. *Streptococcus pyogenes* is a toxigenic bacterium causing a variety of diseases. Which of the following statements best characterizes this organism?

a. It secretes erythrogenic toxin that causes the characteristic signs of scarlet fever
b. It produces toxin that blocks protein synthesis in an infected cell and carries a lytic bacteriophage that produces the genetic information for toxin production
c. It produces at least one protein toxin consisting of two subunits, A and B, that cause severe spasmodic cough usually in children
d. It has capsules of polyglutamic acid, which is toxic when injected into rabbits
e. It secretes exotoxin that has been called "verotoxin" and "Shiga-like toxin"; infection is mediated by specific attachment to mucosal membranes

221. *N. meningitidis* causes meningitis in all age groups. A characteristic physiological trait is that it

a. Possesses *N*-acetylneuraminic acid capsule and adheres to specific tissues by pili found on the bacterial cell surface
b. Has capsule of polyglutamic acid, which is toxic when injected into rabbits
c. Synthesizes protein toxin as a result of colonization of vaginal tampons
d. Causes spontaneous abortion and has tropism for placental tissue due to the presence of erythritol in allantoic and amniotic fluid
e. Secretes two toxins, A and B, in large bowel during antibiotic therapy

222. *Brucella* is pathogenic for humans and animals. Which one of the following statements best characterizes this organism?

a. It has capsule of polyglutamic acid, which is toxic when injected into rabbits
b. It synthesizes protein toxin as a result of colonization of vaginal tampons
c. It causes spontaneous abortion and has tropism for placental tissue due to the presence of erythritol in allantoic and amniotic fluid
d. It secretes two toxins, A and B, in large bowel during antibiotic therapy
e. It has 82 polysaccharide capsular types; capsule is antiphagocytic; type 3 capsule (b-d-glucuronic acid polymer) most commonly seen in infected adults

Questions 223–227

An 18-year-old male patient appeared at the emergency room with a 3-day history of fever, dry cough, difficulty breathing, and muscle aches and pains. His chest x-ray showed a diffuse left upper lobe infiltrate. The following 5 questions focus on the etiology of "atypical" or community-acquired pneumonia:

223. *Mycoplasma pneumoniae* pneumonia (walking pneumonia) may be rapidly identified by which of the following procedures?

a. Detection of specific antigen in urine
b. Cold agglutinin test
c. Electron microscopy of sputum
d. Culture of respiratory secretions in HeLa cells after centrifugation of the inoculated tubes
e. Culture of respiratory secretions on monkey kidney cells

224. Influenza can be treated; therefore, specific detection of the virus becomes much more important. Which of the following would be best for detection of influenza?

a. Detection of specific antigen in urine
b. Cold agglutinin test
c. Electron microscopy of sputum
d. Detection of antigen in respiratory secretions
e. Culture of respiratory secretions on monkey kidney cells

225. Legionnaires' disease is most rapidly diagnosed by which one of the following procedures?

a. Detection of specific antigen in urine
b. Cold agglutinin test
c. Electron microscopy of sputum
d. Detection of antigen in respiratory secretions
e. Culture of respiratory secretions on a charcoal-based nutrient agar.

226. *Chlamydia pneumoniae* has recently been implicated in respiratory disease primarily in children. Which of the following would best isolate this fastidious bacterium?

a. Detection of specific antigen in urine
b. Cold agglutinin test
c. Electron microscopy of sputum
d. Culture of respiratory secretions in HeLa cells after centrifugation of the inoculated tubes
e. Culture of respiratory secretions on monkey kidney cells

227. *Bordetella* bronchitis, sometimes called whooping cough, can best be detected by which of the following procedures?

a. Fluorescent antibody detection of the organism in sputum
b. Cold agglutinin test
c. Direct microscopy of sputum by Gram stain
d. Culture of respiratory secretions in HeLa cells after centrifugation of the inoculated tubes
e. Culture of respiratory secretions on Regan-Lowe agar

Bacteriology

Answers

116. The answer is d. *(Howard, p 457.) Helicobacter pylori* was first recognized as a possible cause of gastritis and peptic ulcer by Marshall and Warren in 1984. This organism is readily isolated from gastric biopsies but not from stomach contents. It is similar to *Campylobacter* species and grows on chocolate agar at 37°C in the same microaerophilic environment suitable for *C. jejuni* (Campy-Pak or anaerobic jar [Gas Pak] without the catalyst). *H. pylori,* however, grows more slowly than *C. jejuni,* requiring 5 to 7 days incubation. *C. jejuni* grows optimally at 42°C, not 37°C, as does *H. pylori.*

117. The answer is d. *(Raoult, pp 446–447.)* The major determinant of virulence in *H. influenzae* is the presence of a capsule. There is no demonstrable exotoxin and the role of endotoxin is unclear. While one would expect that IgA protease would inhibit local immunity, the role of this enzyme in pathogenesis is as yet unclear.

118. The answer is a. *(Raoult, pp 1084–1085.)* The toxin of *V. cholerae* and LT enterotoxin from *Escherichia coli* are similar. The B subunits of the toxins bind to ganglioside GM1 receptors on the host cell. The A subunits catalyze transfer of the ADP-ribose moiety of ADP to a regulatory protein known as Gs. This activated Gs stimulates adenyl cyclase. Cyclic AMP is increased as is fluid and electrolyte release from the crypt cells into the lumen of the bowel. Watery, profuse diarrhea ensues.

119. The answer is c. *(Raoult, pp 574–575.)* Leprosy (Hansen's disease) affects primarily skin, peripheral nerves, and mucous membranes. The disease ranges from tuberculoid leprosy, which is characterized by few lesions containing small numbers of acid fast mycobacteria, to lepromatous leprosy, which is characterized by multiple lesions containing many microorganisms. Chronic pulmonary infection is more characteristic of infection with *Mycobacterium tuberculosis* than *M. leprae.*

120–121. The answers are 120-e, 121-b. *(Levinson, pp 30, 106.)* There have been a number of outbreaks of food poisoning caused by *Listeria*

monocytogenes. *Listeria* is a common inhabitant of farm animals and can be readily isolated from silage, hay, and barnyard soil. Humans at the extremes of age are most susceptible to *Listeria* infection but only recently has food been implicated as a vehicle. In the outbreak in Nova Scotia, it is likely that the cabbage used for the coleslaw was fertilized with animal droppings and not properly washed prior to consumption. Major *Listeria* outbreaks associated with cheese have been seen in the United States and most likely have originated from contaminated milk. Epidemiologic investigation often will provide data on attack rates in such outbreaks. The eventual solution of the problem always lies in a combination of epidemiologic, microbiologic, and clinical information. For example, in the Nova Scotia case, it should not be assumed that the eclairs were the culprit based on the fact that everyone ate them.

122–124. The answers are 122-a, 123-a, 124-c. *(Levinson, pp 143–144.) Mycoplasma pneumoniae* causes a respiratory infection known as primary atypical pneumonia or walking pneumonia. Although disease caused by *M. pneumoniae* can be contracted year-round, thousands of cases occur during the winter months in all age groups. The disease, if untreated, will persist for 2 weeks or longer. Rare but serious side effects include cardiomyopathies and central nervous system complications. Infection with *M. pneumoniae* may be treated with either erythromycin or tetracycline. The organism lacks a cell wall and so is resistant to the penicillin and the cephalosporin groups of antibiotics.

Until recently, diagnostic tests have been of limited value. Up to 50% of cases may not show cold agglutinins, an insensitive and nonspecific acute-phase reactant. However, if cold agglutinins are present, a quick diagnosis can be made if signs and symptoms are characteristic. Complement fixation tests that measure an antibody to a glycolipid antigen of *M. pneumoniae* are useful but not routinely performed in most laboratories. Also, cross-reactions may occur. Culture of *M. pneumoniae,* while not technically difficult, may take up to 2 weeks before visible growth is observed. A DNA probe is available. It is an 125I probe for the 16S ribosomal RNA of *M. pneumoniae*. Evaluations in a number of laboratories indicate that compared with culture it is highly sensitive and specific.

125. The answer is c. *(Raoult, pp 673–674.)* Most cases of tuberculosis are caused when patients inhale droplet nuclei containing infectious organisms. While the bacilli are deposited on the alveolar spaces, they do not clog up the

alveoli but are engulfed by macrophages. Tissue injury is not a result of toxin secretion but by cell-mediated hypersensitivity, that is, "immunologic injury."

126. The answer is a. *(Murray, pp 1481–1483.)* A new class of antibiotics, the quinolones, has one member, nalidixic acid, that has been available for years. The new representatives are much more active biologically and are effective against virtually all Gram-negative bacteria and most Gram-positive bacteria. They include norfloxacin, ofloxacin, ciprofloxacin, enoxacin, and the fluorinated quinolones such as lomefloxacin. These antibiotics kill bacteria by inhibition of synthesis of nucleic acid, more specifically, DNA gyrase. Resistance to quinolones has been observed and appears to be a class-specific phenomenon. An exception is when an organism is resistant to nalidixic acid, elevated minimal inhibitory concentrations (MICs) will generally apply to other quinolones, although these MICs will still be within the range of susceptibility.

127. The answer is c. *(MMWR September 5, 1997, vol 46 No 35 pp 813–815.)* Vancomycin-indeterminate *Staphylococcus aureus* (VISA) were first recognized in Japan. Emergence in the United States soon followed. It is likely that the human VISA isolates have resulted from increased use of vancomycin for patients with MRSA or perhaps an increased pool of VISA in the environment selected out by the use of glycopeptides such as avoparcin, a growth promoter used in food producing animals. In patients with VISA, the Centers for Disease Control (CDC) strongly recommends compliance with isolation procedures and other infection control practices geared to control of VISA.

128. The answer is e. *(Howard, pp 213–242.)* Many sputum specimens are cultured unnecessarily. Sputum is often contaminated with saliva or is almost totally made up of saliva. These specimens rarely reveal the cause of the patient's respiratory problem and may provide laboratory information that is harmful. The sputum in question appears to be a good specimen. The pleomorphic Gram-negative rods are suggestive of *Haemophilus,* but culture of the secretions is necessary.

129. The answer is a. *(Levinson, pp 124–125.) Bacteroides fragilis* is a constituent of normal intestinal flora and readily causes wound infections often mixed with aerobic isolates. These anaerobic, Gram-negative rods are uniformly resistant to aminoglycosides and usually to penicillin as well.

Reliable laboratory identification may require multiple analytical techniques. Generally, wound exudates smell bad owing to production of organic acids by such anaerobes as *B. fragilis.* Black exudates or a black pigment (heme) in the isolated colony is usually a characteristic of *Bacteroides* (*Porphyromonas*) *melaninogenicus,* not *B. fragilis.* Potent neurotoxins are synthesized by the Gram-positive anaerobes such as *Clostridium tetani* and *C. botulinum.*

130. The answer is c. *(Levinson, pp 4–7.)* Bacterial cell walls are complex macromolecular structures. While there are differences between Gram-negative and Gram-positive cell walls (e.g., teichoic acid), the structure of peptidoglycan is common except for differences in the extent of cross-linking in various species and the structures that are cross-linked. A peptidoglycan with a different structure has been discovered in Archaebacteria. This macromolecule contains talosaminuronic acid instead of muramic acid.

131. The answer is a. *(Raoult, pp 586–587.) Listeria* multiply both extracellularly and intracellularly, but under most circumstances a competent immune system eliminates *Listeria.* As expected, listeriosis is seen in the very young, the very old, and in people with compromised immune systems. Reports of *Listeria* food outbreaks have implicated such foods as coleslaw and milk products.

132–135. The answers are 132-b, 133-b, 134-b, 135-c. *(Levinson, pp 145–147.)* This patient appears to have primary syphilis as evidenced by a penile chancre that was not tender. One of the differences between syphilis and herpes simplex virus (HSV) is that an HSV lesion is excruciatingly painful. Treponemal organisms may be seen microscopically in the lesion if the lesion is scraped. If not treated, the chancre will disappear and the patient will be asymptomatic until he/she exhibits the signs/symptoms of secondary syphilis, which include a disseminated rash and systemic involvement such as meningitis, hepatitis, or nephritis. There are two kinds of tests for the detection of syphilis antibodies: nonspecific tests such as the RPR and VDRL, and specific tests such as the FTA, TPHA (Treponema pallidum hemagglutination test), and the MHTP (microhemagglutination-T. pallidum). The difference is that the nonspecific tests use a cross-reactive antigen known as cardiolipin, while the specific tests use a *T. pallidum* antigen. Although the nonspecific tests are sensitive, they lack specificity and often cross-react in patients who have

diabetes, hepatitis, infectious mononucleosis, or who are pregnant. Some patients, especially those with autoimmune diseases, will have both nonspecific (RPR) and specific tests (FTA) positive. Resolution of such a situation can be done by molecular methods for *T. pallidum* such as PCR, or by the immobilization test using live spirochetes and the patient's serum. In the TPI test, the spirochetes will die in the presence of specific antibody.

136. The answer is c. *(Levinson, pp 143–144.)* The symptoms of Legionnaires' disease are similar to those of mycoplasmal pneumonia and influenza. Affected persons are moderately febrile, complain of pleuritic chest pain, and have a dry cough. Unlike *Klebsiella* and *Staphylococcus, Legionella pneumophila* exhibits fastidious growth requirements. Charcoal yeast extract agar either with or without antibiotics is the preferred isolation medium. While sputum may not be the specimen of choice for *Legionella,* the discovery of small Gram-negative rods by direct fluorescent antibody (FA) technique should certainly heighten suspicion of the disease. *L. pneumophila* is a facultative intracellular pathogen and enters macrophages without activating their oxidizing capabilities. The organisms bind to macrophage C receptors, which promote engulfment.

137. The answer is c. *(Howard, pp 416–417.)* Patients treated with antibiotics develop diarrhea that, in most cases, is self-limiting. However, in some instances, particularly in those patients treated with ampicillin or clindamycin, a severe, life-threatening pseudomembranous enterocolitis develops. This disease has characteristic histopathology, and membranous plaques can be seen in the colon by endoscopy. Pseudomembranous enterocolitis and antibiotic-associated diarrhea are caused by an anaerobic Gram-positive rod, *Clostridium difficile*. It has been recently shown that *C. difficile* produces a protein toxin with a molecular weight of about 250,000. The "toxin" is, in fact, two toxins, toxin A and toxin B. Both toxins are always present in fecal samples, but there is approximately one thousand times more toxin B than toxin A. Toxin A has enterotoxic activity—that is, it elicits a positive fluid response in ligated rabbit ileal loops—whereas toxin B appears to be primarily a cytotoxin.

138. The answer is c. *(Baron, pp 163–186.)* The interpretation of quantitative antimicrobial susceptibility tests is based on both the minimal inhibitory concentration (MIC) and the achievable blood level of a given

antibiotic. An MIC greater than the achievable blood concentration of an antibiotic suggests resistance. An MIC at or near the achievable level is equivocal, and an MIC significantly lower than the achievable level—say, by 75%—suggests susceptibility of the isolate to the antibiotic being tested. Thus, *Klebsiella* listed in the question as having an MIC of 0.25 mcg/mL is susceptible to gentamicin with an average serum level of 6 to 8 mcg/mL.

139. The answer is c. *(Levinson, pp 133–134.) Pasteurella multocida,* a coccobacillary Gram-negative rod, is part of the normal mouth flora of dogs and cats. Consequently, many animal bites become infected with this microorganism. It is susceptible to penicillin, although multiresistant strains have been recovered from pigs and sheep. *P. multocida* has four different capsular types—designated A, B, D, and E—that correlate with disease production and host predilection; however, serotyping of these isolates is beyond the resources of most laboratories.

140. The answer is a. *(Baron, pp 441–450.)* The patient presented with typical symptoms of actinomycosis. *Actinomyces israelii* is normal flora in the mouth. However, it causes a chronic draining infection, often around the maxilla or the mandible, with osteomyelitic changes. Treatment is high-dose penicillin for 4 to 6 weeks. The diagnosis of actinomycosis is often complicated by the failure of *A. israelii* to grow from the clinical specimen. It is an obligate anaerobe. Fluorescent antibody (FA) reagents are available for direct staining of *A. israelii.* A rapid diagnosis can be made from the pus. FA conjugates are also available for *A. viscosus* and *A. odontolyticus,* anaerobic actinomycetes that are rarely involved in actinomycotic abscesses.

141–143. The answers are 141-a, 142-a, 143-d. *(Ryan, pp 276–277.)* The incidence of group B streptococcal disease (GBS) is 1–3 cases per 1000 births. Neonates acquire the disease during birth from mothers who harbor the organism. Risk factors include prematurity, premature rupture of membranes, and group B streptococcal carriage. The Gram's stain of cerebrospinal fluid is a rapid test for GBS disease. Although sensitive, the Gram's stain requires experience to differentiate these streptococci from other Gram-positive cocci. Latex tests for GBS antigen are also available, but sensitivity in CSF is not significantly higher than the Gram's stain. GBS can be reduced by intrapartum administration of penicillin. Experimentally, GBS polysaccharide vaccines have also been used. Screening pregnant females early in pregnancy probably offers little advantage because of the

possible acquisition of GBS late in the pregnancy. There has been speculation concerning the pathogenesis of GBS. These include failure to activate complement pathways and immobilization of polymorphonuclear leukocytes (PMNs) due to the inactivation of complement C5A, a potent chemoattractant. While GBS is relatively more resistant to penicillin than group A streptococci, the great majority of GBS isolates are still penicillin-susceptible. An aminoglycoside such as gentamicin may be added to GBS treatment regimens due to the relative reduced susceptibility of some strains.

144. The answer is c. *(Levinson, pp 52–54, 146–147.)* In men, the appearance of a hard chancre on the penis characteristically indicates syphilis. Even though the chancre does not appear until the infection is 2 or more weeks old, the VDRL test for syphilis still can be negative despite the presence of a chancre (the VDRL test may not become positive for 2 or 3 weeks after initial infection). However, a lesion suspected of being a primary syphilitic ulcer should be examined by dark-field microscopy, which can reveal motile treponemes.

145. The answer is a. *(Levinson, pp 130–131.) Brucella* are small, aerobic, Gram-negative coccobacilli. Of the four well-characterized species of *Brucella,* only one—*B. melitensis*—characteristically infects both goats and humans. Brucellosis may be associated with gastrointestinal and neurologic symptoms, lymphadenopathy, splenomegaly, hepatitis, and osteomyelitis.

146. The answer is e. *(Levinson, pp 118–119.)* Cholera is a toxicosis. The mode of action of cholera toxin is to stimulate the activity of adenyl cyclase, an enzyme that converts ATP to cyclic AMP. Cyclic AMP stimulates the secretion of chloride ion, and affected patients lose copious amounts of fluid. A drug that inhibits adenyl cyclase thus might block the effect of cholera toxin.

147. The answer is a. *(Howard, pp 231–250.)* Certain strains of staphylococci elaborate an enterotoxin that is frequently responsible for food poisoning. Typically, the toxin is produced when staphylococci grow on foods rich in carbohydrates and is present in the food when it is consumed. The resulting gastroenteritis is dependent only on the ingestion of toxin and not on bacterial multiplication in the gastrointestinal tract. Characteristic symptoms are nausea, vomiting, abdominal cramps, and explosive diarrhea. The illness rarely lasts more than 24 h.

148. The answer is b. *(Levinson, pp 85–89.)* Staphylococci are Gram-positive, non-spore-forming cocci. Clinically, their antibiotic resistance poses major problems. Many strains produce β-lactamase (penicillinase), an enzyme that destroys penicillin by opening the lactam ring. Drug resistance, mediated by plasmids, may be transferred by transduction.

149. The answer is d. *(Levinson, pp 102–103.) Clostridium botulinum* growing in food produces a potent neurotoxin that causes diplopia, dysphagia, respiratory paralysis, and speech difficulties when ingested by humans. The toxin is thought to act by blocking the action of acetylcholine at neuromuscular junctions. Botulism is associated with high mortality; fortunately, *C. botulinum* infection in humans is rare.

150. The answer is d. *(Howard, pp 323–324.)* Many types of infection, notably respiratory tract infections and osteomyelitis, are common in people who have sickle cell anemia. For unknown reasons, *Salmonella* is implicated frequently in these infections. Osteomyelitis in other persons is caused most often by *Staphylococcus.*

151. The answer is a. *(Levinson, pp 119–120.)* Until recently, both erythromycin and ciprofloxacin were the drugs of choice for *C. jejuni* enterocolitis. Recently, resistance to the quinolones (ciprofloxacin) has been observed. Ampicillin is ineffective against this Gram-negative curved rod. While Pepto-Bismol may be adequate for a related ulcer-causing bacterium, *Helicobacter,* it is not used for *C. jejuni.* While the pathogenesis of *C. jejuni* suggests an enterotoxin, an antitoxin is not available.

152. The answer is d. *(Levinson, pp 126–127.) Haemophilus influenzae* is a Gram-negative bacillus. In young children, it can cause pneumonitis, sinusitis, otitis, and meningitis. Occasionally, it produces a fulminative laryngotracheitis with such severe swelling of the epiglottis that tracheostomy becomes necessary. Clinical infections with this organism after the age of 3 years are less frequent.

153–155. The answers are 153-d, 154-e, 155-e. *(Ryan, pp 282–283.)* Enterococci causes a wide variety of infections ranging from less serious, for example, urinary tract infections, to very serious, such as septicemia. A Gram-positive coccus resistant to penicillin must be assumed to be entero-

coccus until other more definitive biochemical testing places the isolate in one of the more esoteric groups of Gram-positive cocci. Once isolated, there are a variety of tests to speciate enterococci. However, penicillin-resistant, non-β-lactamase-producing, vancomycin-resistant, Gram-positive cocci are most likely *Enterococcus faecium.* There are a variety of mechanisms for vancomycin resistance in *E. faecium* and they have been termed Van A, B, or C. These isolates have become one of the most feared nosocomial pathogens in the hospital environment. Unfortunately, no approved antibiotics can successfully treat vancomycin-resistant enterococci (VRE), only some experimental antibiotics such as Synercid.

156. The answer is d. *(Levinson, p 87.) Staphylococcus aureus* is implicated in the majority of cases of acute osteomyelitis, which affects children most often. A superficial staphylococcal lesion frequently precedes the development of bone infection. In the preantibiotic era, *S. pneumoniae* was a common cause of acute osteomyelitis. *Mycobacterium tuberculosis* and Gram-negative organisms are implicated less frequently in this infection.

157. The answer is c. *(Howard, pp 429–430.)* All toxigenic strains of *Corynebacterium diphtheriae* are lysogenic for β-phage carrying the Tox gene, which codes for the toxin molecule. The expression of this gene is controlled by the metabolism of the host bacteria. The greatest amount of toxin is produced by bacteria grown on media containing very low amounts of iron.

158–160. The answers are 158-b, 159-a, 160-c. *(Raoult, pp 976–977.)* Toxic shock syndrome (TSS) is a febrile illness seen predominantly, but not exclusively, in menstruating women. Clinical criteria for TSS include fever greater than 102°F (38.9°C), rash, hypotension, and abnormalities of the mucous membranes and the gastrointestinal, hepatic, muscular, cardiovascular, or central nervous system. Usually three or more systems are involved. Treatment is supportive, including the aggressive use of antistaphylococcal antibiotics. Certain types of tampons may play a role in TSS by trapping O_2 and depleting magnesium. Most people have protective antibodies to the toxic shock syndrome toxin (TSST-1).

Toxic shock syndrome (TSS) is caused by a toxin-producing strain of *Staphylococcus aureus* (TSST-1). While there have been reports that *S. epidermidis* produces TSS, they have largely been discounted. Vaginal colonization

with *S. aureus* is a necessary adjunct to the disease. *S. aureus* is isolated from the vaginal secretions, conjunctiva, nose, throat, cervix, and feces in 45 to 98% of cases. The organism has infrequently been isolated from the blood.

Epidemiologic investigations suggest strongly that toxic shock syndrome is related to use of tampons, in particular, use of the highly absorbent ones that can be left in for extended periods of time. An increased growth of intravaginal *S. aureus* and enhanced production of TSST-1 have been associated with the prolonged intravaginal use of these hyperabsorbent tampons and with the capacity of the materials used in them to bind magnesium. The most severe cases of TSS have been seen in association with Gram-negative infection. TSST-1 may enhance endotoxin activity. Recently, group A streptococci have been reported to cause TSS.

161–164. The answers are 161-c, 162-d, 163-c, 164-b. *(Murray, pp 110–111.)* Bayesian statistics are often used to determine sensitivity, specificity, and predictive values of new diagnostic tests. A square is set up and the experimental numbers inserted: a = true positive, b = false positive, c = false negative, and d = true negative. The formulas for sensitivity, specificity, and predictive values are also given.

	Culture	
LA Test	**POS**	**NEG**
POS	(a) 25	(b) 5
NEG	(c) 5	(d) 95

$$\text{Sensitivity} = \frac{a}{a+c} = \frac{25}{25+5} = 85\%$$

$$\text{Specificity} = \frac{d}{d+b} = \frac{95}{95+5} = 95\%$$

$$\text{PVP} = \frac{a}{a+b} = \frac{25}{25+5} = 85\%$$

$$\text{PVN} = \frac{d}{d+c} = \frac{95}{95+5} = 95\%$$

It is necessary to note that the incidence of the disease in the population affects predictive values but not sensitivity or specificity. At a given

level of sensitivity and specificity, as the incidence of the disease in the population increases, the predictive value of a positive (PVP) increases, and the predictive value of a negative (PVN) decreases. For this reason, predictive values are difficult to interpret unless true disease incidence is known.

165. The answer is b. *(Howard, pp 253–254.)* Oxacillin- and methicillin-resistant *S. aureus* (MRSA) has been rapidly increasing in incidence. MRSA and methicillin-sensitive *S. aureus* (MSSA) coexist in heterologous populations. Treatment of a patient harboring this heterologous population may provide a selective environment for the MRSA. Prior to changing therapy, the susceptibility of the isolate should be determined. Vancomycin has often been used effectively for MRSA, but it is expensive and nephrotoxic. There is no evidence that MRSA is any more virulent or invasive than susceptible strains.

166. The answer is a. *(Howard, pp 479–480.)* Coccidian-like bodies have been identified in stools of some patients with diarrhea. These organisms appear to be similar to blue-green algae and were referred to as *Cyanobacterium*-like until they were recently reclassified as *Cyclospora.* They are larger than the microsporidia and resemble neither *Giardia* nor *Prototheca* nor other algae-like organisms. Unlike *Cryptosporidium,* these organisms fluoresce under ultraviolet light.

167. The answer is d. *(Howard, pp 322, 325–328.)* Food poisoning with *E. coli* 0157/H7 causes hemorrhagic colitis; it is often seen after eating beef hamburgers. The same organism also causes a hemorrhagic uremic syndrome. The toxin, called *Shiga-like toxin,* can be demonstrated in Vero cells, but the cytotoxicity must be neutralized with specific antiserum. With the exception of sorbitol fermentation, there is nothing biochemically distinctive about these organisms.

168. The answer is b. *(Howard, pp 322, 325–328.)* LT and ST proteins are characteristic of enterotoxigenic *E. coli.* To cause diarrhea, *E. coli* must produce not only LT and ST toxins but also adhere to the lining of the small intestine. Fimbrial antigens are involved in adherence.

169. The answer is b. *(Howard, p 325.)* Bubonic plague and pneumonic plague differ clinically. Bubonic plague, characterized by swollen lymph

nodes and fever, is usually transmitted through a flea bite. Pneumonic plague, which is characterized by sepsis and pneumonia, is transmitted by the droplet route usually after contact with an infected human or animal.

170. The answer is e. *(Howard, p 860.)* While the essential information (i.e., the evidence that the child in question was scratched by a cat) is missing, the clinical presentation points to a number of diseases, including cat-scratch disease (CSD). Until recently, the etiologic agent of CSD was unknown. Evidence indicated that it was a pleomorphic, rod-shaped bacterium that had been named *Afipia.* It was best demonstrated in the affected lymph node by a silver impregnation stain. However, it now appears that *Afipia* causes relatively few cases of CSD and that the free-living rickettsia primarily responsible is *Rochalimaea henselae,* which has recently been renamed *Bartonella henselae.*

171. The answer is b. *(Howard, pp 284–285.)* There has been a marked increase in fatal streptococcal infections including those that are described as "necrotizing fasciitis." The strains of group A streptococci isolated have a pyrogenic exotoxin with properties not unlike those of the toxic shock toxin of *S. aureus.* Mortality is high (30%) in spite of aggressive antibiotic therapy.

172. The answer is a. *(Ryan, pp 351–352.) H. pylori* antigen tests using an ELISA format and a monoclonal antibody to *H. pylori* are as sensitive as culture of the control portion of the stomach. Urea breath tests are also widely used. *H. pylori* has an active enzyme (urease) which breaks down radioactive urea. The patient releases radioactive CO_2 if *H. pylori* are present. *H. pylori* antibody tests, IgG and IgA, indicate the presence of *H. pylori* and usually decline after effective treatment. Culture of stomach contents is insensitive and not appropriate as a diagnostic procedure for *H. pylori.* Direct tests such as antigen or culture of gastric mucosa are preferred because they are the most sensitive indication of a cure.

173. The answer is c. *(Levinson, pp 147–148.)* At the present time, Lyme disease may be diagnosed clinically and serologically. Patients who are from endemic areas such as eastern Pennsylvania and report joint pain and swelling months subsequent to exposure to ticks must be evaluated for Lyme disease and treated if the test is positive. Patients may also report a variety of neurologic problems such as tingling of the extremities, Bell's palsy, and headache. IgM antibody appears soon after the tick bite (10

days to 3 weeks) and persists for 2 months; IgG appears later in the disease but remains elevated for 1 to 2 years, especially in untreated patients. A significant IgG titer is at least 1:320. Most investigators feel that IgM titers of 1:100 are significant; some investigators say that any IgM titer is significant.

174. The answer is e. *(Levinson, pp 134–139.)* There are some interesting characteristics of *Mycobacterium avium* from AIDS patients. According to data from the National Jewish Hospital and Research Center in Denver and the Centers for Disease Control, 75% of the isolates were serovar 4, and 76% produced a deep-yellow pigment. Yellow pigment is not a characteristic of most isolates of *M. avium.* The significance of these findings is unknown. Most *M. avium* isolates are resistant to isoniazid and streptomycin but susceptible to clofazimine and ansamycin. In vitro susceptibility testing, however, may not be reliable for *M. avium.* A blood culture is often the most reliable way to diagnose the disease.

175. The answer is a. *(Howard, p 266.)* Rheumatic fever (RF) is a disease that causes polyarthritis, carditis, chorea, and erythema marginatum. The mechanism of damage appears to be autoimmune; that is, antibodies are synthesized to a closely related streptococcal antigen such as M-protein, but these same antibodies cross-react with certain cardiac antigens such as myosin. Until recently, RF was very rare in the United States. In 1986, there were at least 135 cases of RF in Utah. Subsequently, scattered cases of RF have occurred in other states. Epidemiologists do not have a reason for this increase in RF. Some evidence suggests that there may be a genetic predisposition to the disease. Intramuscular injection of benzathine penicillin is effective treatment for and prophylaxis against group A streptococcal infection.

176. The answer is b. *(Levinson, pp 96–99.)* Pathogenic neisseriae (*Neisseria meningitidis, N. gonorrhoeae*) will not grow on plain agar; they grow best on blood-enriched plates in the presence of 10% carbon dioxide. *Branhamella catarrhalis* and *N. sicca* grow on plain nutrient agar. *N. meningitidis* (strain A in the question) produces acid from maltose and dextrose, whereas *N. gonorrhoeae* (strain B) ferments only dextrose. Strain C could be either *B. catarrhalis* or *N. flavescens. N. sicca* (strain D) produces acid from sucrose, maltose, and dextrose. *B. catarrhalis* is known to be an etiologic agent of pneumonia, while *N. sicca* is normal flora.

177. The answer is a. *(Howard, pp 77, 114.)* The quellung test determines the presence of bacterial capsules. Specific antibody is mixed with the bacterial suspension or with clinical material. The polysaccharide capsule–antibody complex is visible microscopically. The test is also termed *capsular swelling.* The capsules of *S. pneumoniae* as well as *N. meningitidis, H. influenzae,* and *K. pneumoniae* play a role in the pathogenicity of the organisms. These surface structures inhibit phagocytosis, perhaps by preventing attachment of the leukocyte pseudopod. *C. diphtheriae, Enterobacter,* and *H. parainfluenzae* are nonencapsulated.

178. The answer is b. *(Howard, pp 32, 252–253, 268.)* Protein exotoxins are diffusible substances elaborated chiefly by Gram-positive organisms, whereas lipopolysaccharide endotoxins are cell-wall components of certain Gram-negative bacteria. The exotoxins of *C. tetani* and *C. botulinum* act directly on the nervous system. Botulium toxin (botox), because of its characteristic mode of action, has been widely used to treat a variety of musculoskeletal problems such as relief of torsion in the neck muscles. The "Shiga toxin" of *Shigella* dysentery acts on the smaller cerebral blood vessels. Diphtheria exotoxin affects body cells in general. Disseminated intravascular coagulation (DIC) results from many conditions, including the action of Gram-negative bacterial endotoxin on the intrinsic clotting system.

179. The answer is c. *(Howard, pp 285–286.)* Except during a meningococcal epidemic, *H. influenzae* is the most common cause of bacterial meningitis in children. The organism is occasionally found to be associated with respiratory tract infections or otitis media. *H. influenzae, N. meningitidis, S. pneumoniae,* and *Listeria* account for 80 to 90% of all cases of bacterial meningitis. A purified polysaccharide vaccine conjugated to protein for *H. influenzae* type B is available. A tetravalent vaccine is available for *N. meningitidis* and a 23-serotype vaccine for *S. pneumoniae.* No vaccine is available for *Listeria.*

180–183. The answers are 180-a, 181-c, 182-b, 183-d. *(Levinson, pp 28–29.)* Organisms may be transmitted in a number of ways, such as by air, food, hands, sexual contact, and infected needles. However, for each disease or disease category, there is usually a portal of entry not always unique to the organism. The respiratory tract is a common portal of entry to such airborne organisms as *M. tuberculosis.* This is why respiratory precautions must be taken when patients are harboring viable *M. tuberculosis.*

The gastrointestinal tract is usually infected from ingestion of contaminated food or water (*Shigella, Salmonella, Campylobacter*) or by an alteration of the normal microbial flora such as with *C. difficile* disease. The skin is a tough integument and, intact, is resistant to most infectious organisms except those that may break down human skin. Breaches of the skin as by wounds, burns, and the like predispose patients to a variety of infections such as tetanus caused by wound contamination with spores of *C. tetani,* or direct infection by *Staphylococcus, Streptococcus,* or Gram-negative rods (such as *Serratia* or *Pseudomonas*). The genital tract may become infected either by sexual contact or by alteration of the genital environment as often occurs with yeast infections. Several bacteria such as *N. gonorrhoeae, Chlamydia,* and *Treponema pallidum* are transmitted by direct sexual contact with infected partners.

184–186. The answers are 184-e, 185-a, 186-c. *(Levinson, pp 156–161.)* While admittedly rare in human medicine, the bacteria referred to should be appreciated for their role in human disease. *Branhamella* is a Gram-negative diplococcus. It has recently been renamed *Moraxella catarrhalis.* While it is a member of the normal flora, it may cause severe upper and lower respiratory tract infection, particularly in the immunosuppressed patient. Most isolates produce β-lactamase and are resistant to penicillin. *Cardiobacterium,* as the name implies, causes endocarditis. This small Gram-negative pleomorphic rod may take a few days to grow. Infection is usually endogenous in that *Cardiobacterium* is part of the normal flora of the gut. *Capnocytophaga* grows best in a carbon dioxide atmosphere as the name implies. It is isolated frequently from patients with periodontal disease but may also cause septicemia in susceptible patients. Rat-bite fever is caused by *Spirillum* and the agent of cat scratch disease is *B. henselae.*

187–189. The answers are 187-d, 188-b, 189-c. *(Levinson, pp 51–52, 68, 70, 141–142.)* These questions demonstrate commonly occurring clinical infectious diseases and microbiologic problems. Enterococci may be resistant to ampicillin and gentamicin. Vancomycin would be the drug of choice. However, laboratory results do not always correlate well with clinical response. The National Committee on Clinical Laboratory Standards recommends testing enterococci only for ampicillin and vancomycin.

Some symptomatic patients may have 10 leukocytes per mL of urine but relatively few bacteria. The patient is likely infected and the organisms, particularly if in pure culture, should be further processed.

The patient in question 189 probably has actinomycosis. These laboratory data are not uncommon. There is no reason to work up all the contaminating bacteria. A fluorescent microscopy test for *A. israelii* is available. If positive, the FA provides a rapid diagnosis. In any event, it may be impossible to recover *A. israelii* from such a specimen. High-dose penicillin has been used to treat actinomycosis.

190–194. The answers are 190-c, 191-a, 192-e, 193-a, 194-d. *(Murray, pp 1475–1504.)* There are few bacteria for which antimicrobial susceptibility is highly predictable. However, some agents are the drug of choice because of their relative effectiveness. Among the three antibiotics that have been shown to treat legionellosis effectively (erythromycin, rifampin, and minocycline), erythromycin is clearly superior, even though in vitro studies show the organism to be susceptible to other antibiotics.

Penicillin remains the drug of choice for *S. pneumoniae* and the group A streptococci, although a few isolates of penicillin-resistant pneumococci have been observed. Resistance among the pneumococci is either chromosomally mediated, in which case the minimal inhibitory concentrations (MICs) are relatively low, or plasmid-mediated, which results in highly resistant bacteria. The same is generally true for *H. influenzae*. Until the mid-1970s, virtually all isolates of *H. influenzae* were susceptible to ampicillin. There has been a rapidly increasing incidence of ampicillin-resistant isolates, almost 35 to 40% in some areas of the United States. Resistance is ordinarily mediated by β-lactamase, although ampicillin-resistant, β-lactamase-negative isolates have been seen. No resistance to penicillin has been seen in group A streptococci.

C. difficile causes toxin-mediated pseudomembranous enterocolitis as well as antibiotic-associated diarrhea. Pseudomembranous enterocolitis is normally seen during or after administration of antibiotics. One of the few agents effective against *C. difficile* is vancomycin. Alternatively, bacitracin can be used.

Lyme disease, caused by *B. burgdorferi,* has been treated with penicillin, erythromycin, and tetracycline. Treatment failures have been observed. Ceftriaxone has become the drug of choice, particularly in the advanced stages of Lyme disease.

195–198. The answers are 195-d, 196-a, 197-c, 198-b. *(Ryan, pp 345–349.)* Some organisms originally thought to be vibrios, such as *C.*

jejuni, have been reclassified. *C. jejuni,* which grows best at 42°C, has its reservoir in birds and mammals and causes gastroenteritis in humans.

V. cholerae causes cholera, which is worldwide in distribution. The three serotypes for cholera are Ogawa (AB), Inaba (AC), and Hikojima (ABC). The isolate of *V. cholerae* is "string-test"-positive.

V. parahaemolyticus is a halophilic marine vibrio that causes gastroenteritis in humans, primarily from ingestion of cooked seafood. It is lactose-negative, sucrose-negative.

Vibrio vulnificus is also halophilic. It has been suggested that these halophilic vibrios do not belong in the genus *Vibrio* but in the genus *Beneckea. V. vulnificus* is lactose-positive and produces heat-labile, extracellular toxin. Organisms that, unlike *V. cholerae,* do not agglutinate in 0-1 antiserum were once called nonagglutinable (NAG), or noncholera (NC), vibrios. Such a classification can be confusing because *V. vulnificus,* which is an NCV, nevertheless causes severe cholera-like disease. In addition, *V. vulnificus* can produce wound infections, septicemia, meningitis, pneumonia, and keratitis.

199–202. The answers are 199-e, 200-c, 201-a, 202-d. *(Levinson, pp 129–134.)* The organisms described in the questions all are short, ovoid, Gram-negative rods. For the most part, they are nutritionally fastidious and require blood or blood products for growth. These and related organisms are unique among bacteria in that, though they have an animal reservoir, they can be transmitted to humans. Humans become infected by a variety of routes, including ingestion of contaminated animal products (*Brucella abortus* in cattle), direct contact with contaminated animal material or with infected animals themselves (*Y. enterocolitica* and *Bordetella bronchiseptica* in dogs), and animal bites (*Pasteurella multocida* in many different animals). The laboratory differentiation of these microbes may be difficult and must rely on a number of parameters, including biochemical and serologic reactions, development of specific antibody response in affected persons, and epidemiologic evidence of infection.

203–207. The answers are 203-c, 204-d, 205-e, 206-b, 207-a. *(Levinson, pp 49–54.)* The medium of choice for the isolation of pathogenic neisseriae is Thayer-Martin (TM) agar. TM agar is both a selective and an enriched medium; it contains hemoglobin, the supplement Isovitalex, and the antibiotics vancomycin, colistin, nystatin, and trimethoprim.

V. cholerae as well as other vibrios, including *V. parahaemolyticus* and *V. alginolyticus,* are isolated best on thiosulfate citrate bile salts sucrose medium, although media such as mannitol salt agar also support the growth of vibrios. Maximal growth occurs at a pH of 8.5 to 9.5 and at 37°C incubation.

Löwenstein-Jensen slants or plates, which are composed of a nutrient base and egg yolk, are used routinely for the initial isolation of mycobacteria. Small inocula of *M. tuberculosis* can also be grown in oleic acid albumin media; large inocula can be cultured on simple synthetic media.

Löffler's medium, which is very rich, supports the growth of *C. diphtheriae* but suppresses the growth of most other nasopharyngeal microflora. *C. diphtheriae* colonies on this medium appear small, gray, and granular and have uneven edges.

S. aureus grows very well on sheep blood agar, which is made up of a nutrient base and 5 to 8% sheep blood; selective and differential media, such as mannitol salt agar, also are available for *S. aureus.*

208–211. The answers are 208-c, 209-a, 210-e, 211-b. (*Murray, pp 23–32.*) An understanding of normal, or indigenous, microflora is essential in order to appreciate the abnormal. Usually, anatomic sites contiguous to mucous membranes are not sterile and have a characteristic normal flora.

The skin flora differs as a function of location. Skin adjacent to mucous membranes may share some of the normal flora of the gastrointestinal system. Overall, the predominant bacteria on the skin surface are *S. epidermidis* and *Propionibacterium,* an anaerobic diphtheroid.

The gastrointestinal tract is sterile at birth and soon develops a characteristic flora as a function of diet. In the adult, anaerobes such as *B. fragilis* and *Bifidobacterium* may outnumber coliforms and enterococci by a ratio of 1000:1. The colon contains 10^{11} to 10^{12} bacteria per gram of feces.

The mouth is part of the gastrointestinal tract, but its indigenous flora shows some distinct differences. While anaerobes are present in large numbers, particularly in the gingival crevice, the eruption of teeth at 6 to 9 months of age leads to colonization by organisms such as *Streptococcus mutans* and *S. sanguis,* both α-hemolytic streptococci. An edentulous person loses α-hemolytic streptococci as normal flora.

Soon after birth, the vagina becomes colonized by lactobacilli. As the female matures, lactobacilli may still be predominant, but anaerobic cocci, diphtheroids, and anaerobic Gram-negative rods also are found as part of the indigenous flora. Changes in the chemical or microbiologic ecology of

the vagina can have marked effects on normal flora and may promote infection such as vaginitis or vaginosis.

212–215. The answers are 212-d, 213-a, 214-c, 215-e. *(Howard, pp 257–269, 404–410.) Streptococcus salivarius, S. mutans, A. viscosus,* and *A. israelii* are all part of the normal microbiota of the human mouth. Both streptococci are usually β-hemolytic, although nonhemolytic variants may appear, and both are common causes of bacterial endocarditis. *S. mutans* is highly cariogenic (i.e., capable of producing dental caries), in large part because of its unique ability to synthesize a dextran bioadhesive that sticks to teeth. *S. salivarius* settles onto the mucosal epithelial surfaces of the human mouth soon after birth and is often found in the saliva.

Members of the genus *Actinomyces* that are clinically significant can be differentiated by specific fluorescent antibody microscopy as well as a battery of physiologic tests, such as those assessing requirements for oxygen. *Actinomyces* organisms are opportunistic members of the normal oral microbiota. Both *A. israelii* and *A. viscosus* are pathogenic and can cause osteomyelitis in the cervicofacial region. Of the two species, *A. israelii,* which is anaerobic, is the more common causative agent of actinomycosis. *A. viscosus,* a facultative anaerobe, appears to be cariogenic.

216–222. The answers are 216-b, 217-c, 218-d, 219-e, 220-a, 221-a, 222-c. *(Ryan, pp 285–289, 323–328, 366–371. Howard, pp 325–328, 425–432, 445–448.)* Diphtheria, a disease caused by *C. diphtheriae,* usually begins as a pharyngitis associated with pseudomembrane formation and lymphadenopathy. Growing organisms lysogenic for a prophage produce a potent exotoxin that is absorbed in mucous membranes and causes remote damage to the liver, kidneys, and heart; the polypeptide toxin inhibits protein synthesis of the host cell. Although *C. diphtheriae* may infect the skin, it rarely invades the bloodstream and never actively invades deep tissue. Diphtheria toxin (DT) kills sensitive cells by blocking protein synthesis. DT is converted to an enzyme that inactivates elongation factor 2 (EF-2), which is responsible for the translocation of polypeptidyl-tRNA from the acceptor to the donor site on the eukaryotic ribosome. The reaction is as follows:

$$\text{NAD} + \text{EF-2} = \text{ADP-ribosyl} - \text{EF-2} + \text{nicotinamide} + \text{H}^+$$

Bordetella pertussis and *B. parapertussis* are similar and may be isolated together from a clinical specimen. However, *B. parapertussis* does not produce pertussis toxin. Pertussis toxin, like many bacterial toxins, has two subunits: A and B. Subunit A is an active enzyme and B promotes binding of the toxin to host cells.

Francisella tularensis is a short, Gram-negative organism that is markedly pleomorphic; it is nonmotile and cannot form spores. It has a rigid growth requirement for cysteine. Human tularemia usually is acquired from direct contact with tissues of infected rabbits but also can be transmitted by the bites of flies and ticks. *F. tularensis* causes a variety of clinical syndromes, including ulceroglandular, oculoglandular, pneumonic, and typhoidal forms of tularemia.

The pathogenesis of infection with *Escherichia coli* is a complex interrelation of many events and properties. *E. coli* may serve as a model for other members of the Enterobacteriaceae. Some strains of *E. coli* are enteroinvasive (EIEC), some enterotoxic (ETEC), some enterohemorrhagic (EHEC), and others enteropathogenic (EPEC). At the present time, there is little clinical significance in routinely discriminating the various types, with the possible exceptions of the ETEC and the *E. coli* 0157/H7 that are hemorrhagic. *E. coli* 0157/H7 secretes a toxin called verotoxin. The toxin is very active in a Vero cell line. More correctly, the toxin(s) should be called *Shiga-like.*

Streptococcal infection usually is accompanied by an elevated titer of antibody to some of the enzymes produced by the organism. Among the antigenic substances elaborated by group A β-hemolytic streptococci are erythrogenic toxin, streptodornase (streptococcal DNase), hyaluronidase, and streptolysin O (a hemolysin). Streptolysin S is a nonantigenic hemolysin. Specifically, erythrogenic toxin causes the characteristic rash of scarlet fever.

Many factors play a role in the pathogenesis of *N. meningitidis.* A capsule containing *N*-acetylneuraminic acid is peculiar to *Neisseria* and *E. coli* K1. Fresh isolates carry pili on their surfaces, which function in adhesion. *Neisseria* have a variety of membrane proteins, and their role in pathogenesis can only be speculated upon at this time. The lipopolysaccharide (LPS) of *Neisseria,* more correctly called lipooligosaccharide (LOS), is the endotoxic component of the cell.

There are no known toxins, hemolysins, or cell wall constituents known to play a role in the pathogenesis of disease by *Brucella.* Rather, the ability of the organisms to survive within the host phagocyte and to inhibit neutrophil degranulation is a major disease-causing factor. In infectious abortion of cat-

tle caused by *Brucella,* the tropism for placenta and the chorion is a function of the presence of erythritol in allantoic and amniotic fluid.

223–227. The answers are 223-d, 224-a, 225-d, 226-d, 227-e. *(Howard, pp 445–447, 491–500, 848–849.)* "Atypical pneumonia" is an old classification used for respiratory disease that is not lobar and is not "typical." That is, it does not include pneumonia caused by pneumococcus, *Klebsiella, Haemophilus,* or β-hemolytic streptococci that results in a typical lobular infiltrate. In recent years, the atypical pneumonias have become much more frequent than pneumococcal pneumonia. They are characterized by a slower onset with headache, joint pain, fever, and signs of an acute upper respiratory infection. There are usually no signs of acute respiratory distress, but patients report malaise and fatigue. The most common cause of atypical pneumonia is *Mycoplasma pneumoniae.* A quick test for *M. pneumoniae* infection is cold agglutinins. The test may lack both sensitivity and specificity, but it is rapid and readily available compared with culture of *M. pneumoniae* or specific antibody formation.

Particularly in the winter months, influenza must be ruled out. In the early stages of an epidemic, viral isolation in primary monkey cells is used. However, as the epidemic proceeds, diagnosis is usually made clinically or by an increase in antibody titer.

In certain age groups (men over 55 years old), Legionnaires' disease must be ruled out. While direct microscopy, culture, and serology are available, the detection of *Legionella* antigen in urine is the most sensitive test available.

Chlamydia pneumoniae may also cause respiratory infection particularly in, but not limited to, children. Diagnosis is best made by growing these energy-defective bacteria in tissue culture such as HeLa cells. Serology is usually not helpful.

During the winter months, *Bordetella* infection may be quite prevalent, particularly in those patients whose immunizations are not current. Adult *Bordetella* infection may not present with typical whooping cough symptoms and must be differentiated from other forms of acute bronchitis by culture on specific media or direct fluorescent microscopy.

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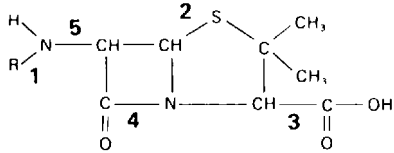
Physiology and Molecular Microbiology

Questions

DIRECTIONS: Each question below contains five suggested responses. Select the **one best** response to each question.

228. Penicillinase isolated from *Staphylococcus aureus* inactivates 6-aminopenicillanic acid (shown below) by breaking which of the following numbered bonds?



a. 1
b. 2
c. 3
d. 4
e. 5

229. Which of the following bacterial transport methods is energy-independent?

a. Facilitated diffusion
b. Simple diffusion
c. Proton gradient energized active transport
d. Group translocation
e. ATP-dependent active transport

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230. Iron is essential in bacterial metabolism. When bacteria invade the human host they must capture iron in order to survive. Which of the macromolecules listed below is important in bacterial iron metabolism?

a. Transferrin
b. Lactoferrin
c. Ferric oxide
d. Lipopolysaccharide (LPS)
e. Siderophores

231. An aliquot of *Escherichia coli* is treated with ethylenediaminetetraacetic acid (EDTA). The first wash is analyzed and found to contain alkaline phosphatase, DNase, and penicillinase. The anatomic area of the cell affected by the EDTA is most likely to have been the

a. Periplasmic space
b. Mesosomal space
c. Chromosome
d. Plasma membrane
e. Slime layer

Questions 232–233

Oxygen is poison to some bacterial cells. These cells are termed *anaerobes.* Other bacteria, termed *aerobes* and *facultative anaerobes,* withstand oxygen toxicity; that is, they can grow in the presence of O_2. The following two equations are critical for bacteria.

$$1.\ 2O^{2-} + 2H^{+} \rightarrow 2H_2O_2 + O_2\cdot$$

$$2.\ H_2O_2 + H_2A^{*} \rightarrow 2H_2O + A$$

232. Reaction 1 is catalyzed by which of the following?

a. Superoxide dismutase
b. ATPase
c. Catalase
d. Peroxidase
e. Oxygen permease

*"A" may be a number of chemical groups

233. Reaction 2 is catalyzed by which of the following?

a. Superoxide dismutase
b. ATPase
c. Peroxidase
d. Oxygen permease
e. Flavoprotein oxidase

234. A bacterium is examined and is found to lack superoxide dismutase, catalase, and peroxidase. Which of the following statements best describes this bacterium?

a. This bacterium is an anaerobe
b. This bacterium will survive in an O_2 environment
c. This bacterium is more virulent than one containing the three enzymes
d. This bacterium does not produce superoxide
e. This bacterium does not produce peroxide

235. Analysis of the metabolites produced by an organism's fermentation of glucose reveals small amounts of 6-phosphogluconic acid. This fermentation organism is most likely to be

a. *Enterobacter*
b. *Escherichia*
c. *Leuconostoc*
d. *Enterococcus faecalis*
e. *Streptococcus lactis*

236. The formation of adenosine triphosphate (ATP) is essential for the maintenance of life. In mammalian systems, the number of moles of ATP formed per gram atom of oxygen consumed (the P/O ratio) is 3; in bacteria, however, the P/O ratio may be only 1 or 2. The primary reason for the lower P/O ratio in bacteria is

a. Absence of nicotinamide adenine dinucleotide (NAD)
b. Loss of oxidative phosphorylation coupling sites
c. Less dependence on ATP as an energy source
d. Absence of a nonphosphorylative bypass reaction
e. A less-efficient mesosome

237. Reversion of *Neisseria gonorrhoeae* from a fimbriated (fim 1) to a nonfimbriated (fim 2) state would result in which one of the following phenomena?

a. Inability of *N. gonorrhoeae* to colonize the mucosal epithelium
b. Reversion to a Gram-positive stain
c. Death of the organism
d. Loss of serologic specificity
e. A negative capsule strain

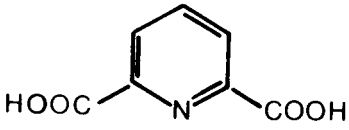
238. An unknown isolate is recognized serologically as *Salmonella enteritidis* serovar newport. A mutant of this organism has lost region 1 (O-specific polysaccharide) of its lipopolysaccharide. This mutant would be identified as

a. *Salmonella typhi*
b. *Salmonella newport*
c. *S. enteritidis*
d. *S. enteritidis* serovar newport
e. *Arizona*

239. Certain enzymes catalyze the cross-linking of peptidoglycan, a unique constituent of bacterial cell walls. Which of the following may be a factor in antibiotic resistance, the target of which is cell-wall synthesis?

a. Bactoprenol
b. Reverse transcriptase
c. RNA polymerase
d. DNA gyrase
e. Penicillin-binding proteins (PBPs)

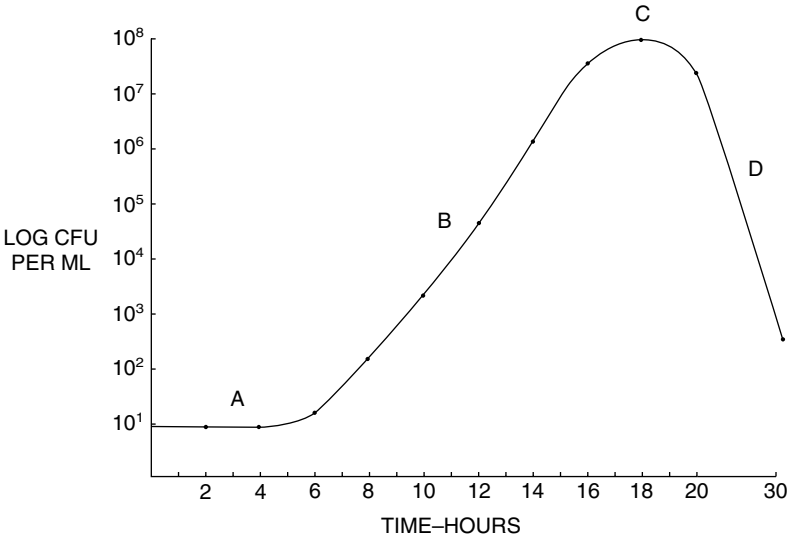
240. Selective inhibition of synthesis of dipicolinic acid (structure shown below) would most likely inhibit the formation of



a. Bacterial flagella
b. Bacterial spores
c. Eukaryotic cilia
d. Eukaryotic flagella
e. Fimbriae

Questions 241–243

Following is the growth curve of *E. coli* growing in a nutrient medium at 35°C with both O_2 and added CO_2 present.



Growth curve—*E. Coli*

The following descriptions are given for the phases of this bacterial growth curve:

a. Lag phase
b. Log phase
c. Stationary phase
d. Death phase

241. In which of the phases would growth not be detectable?

a. Lag phase
b. Log phase
c. Stationary phase
d. Death phase

242. Treatment of the culture with gentamicin, an inhibitor of protein synthesis, would have maximal effect on which of the phases?

a. Lag phase
b. Log phase
c. Stationary phase
d. Death phase

243. If logarithmic growth could be sustained for 48 h, the mass of bacterial cells would equal a volume 500 times that of the planet earth. Which of the following are limiting factors in microbial growth?

a. Accumulation of oxygen free radicals
b. Accumulation of peroxide
c. Accumulation of toxic products in the growth medium
d. Oxygen
e. Loss of superoxide dismutase

244. Ideally, an antibiotic should focus on a microbial target not found in mammalian cells. By this standard, which of the following antibiotic agents would be expected to be most toxic to humans?

a. Penicillin
b. Mitomycin
c. Cephalosporin
d. Bacitracin
e. Vancomycin

245. A freeze-fractured *E. coli* is shown below. The elliptical structure at the left is the

a. Plasma membrane
b. Cell wall
c. Cell capsule
d. Cytoplasm
e. Flagellum

246. *E. coli* has two major porins located in the outer membrane. The function of porins is the

a. Stabilization of the mesosome
b. Metabolism of phosphorylated intermediates
c. Transfer of small molecules through the outer membrane
d. Serologic stabilization of the O antigen
e. Diffusion of safranin from the cell, thereby rendering the cell Gram-negative

247. A 21-year-old man was bitten by a tick in Oregon. Two years later, during the course of routine screening for an unknown ailment, a screening Lyme disease test was performed, which was negative. A Western blot strip (IgG) showed the following pattern:

Which of the following is the correct interpretation of the test?

a. The patient has acute Lyme disease
b. The patient has chronic Lyme disease
c. The pattern may represent nonspecific reactivity
d. The screening test should be repeated
e. The patient should be tested for HIV on the basis of the Western blot

248. Early attempts at the polymerase chain reaction (PCR) used *E. coli* DNA polymerase. This was replaced with DNA polymerase from *Thermus aquaticus* ("Taq" polymerase). The primary advantage in using this enzyme is

a. It is cheaper than *E. coli* polymerase
b. Specificity is increased because nonspecific hybridization of primers does not occur
c. Use of Taq polymerase results in fewer PCR cycles
d. Use of Taq polymerase enables lower temperatures to be used
e. Upon repeated cycling, Taq polymerase becomes denatured, which causes less interference with the hybridization process

Questions 249–251

You have been asked to design a nucleic acid amplification test for a rarely isolated bacterium. There are several questions that you must ask in order to develop a test that could be used to diagnose disease.

249. Assume, initially, that the polymerase chain reaction (PCR) will amplify any DNA, human or microbial. The best way to prevent contamination of the PCR process is to

a. Wear gloves
b. Wash benches with bleach
c. Use universal precautions
d. Incorporate self-sterilizing agents into the PCR mixture
e. Do all of the work under a hood

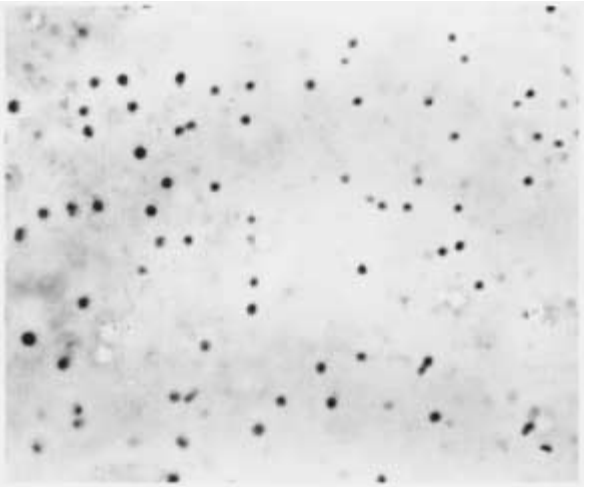
250. You must choose primers for this PCR. *Primers* are small pieces of nucleic acid that recognize a pair of unique sites on the bacterial chromosome. For an optimum test to be developed, which of the following characteristics is the least desirable?

a. Ability to be constructed by a synthesizer
b. Uniqueness to the organism that you wish to detect
c. Complementary to sequences on the bacterial chromosome
d. Ability to serve as a template for replication
e. That the sequences are widely recognized by many bacterial species

251. You have chosen the primers for the PCR that you have designed. You have also developed a reaction mixture that contains, among other substances, a polymerase enzyme. After the primer pairs have been amplified, they must be detected. Which of the following detection methods is most sensitive (that is, will detect the highest number of amplicons)?

a. Southern blot
b. Ethidium staining of the amplified products (amplicons)
c. Microscopy
d. Capture of the amplicons on a solid phase followed by an enzyme immunoassay
e. Labeling of the amplicons with fluorescent dyes

252. Which one of the following statements about the *E. coli* cells shown in the photomicrograph below is true?



a. They can result from treatment with penicillin
b. Treatment of the parent *E. coli* with lysozyme has no effect
c. They are osmotically stable
d. They are commonly referred to as endospores
e. They have formed cell walls but have become coccoid

253. The purpose of gene cloning is to produce large amounts of genes in pure form. The sequence of the cloning process is critical to the production of clones. Which of the following steps initializes the cloning process?

a. Isolation and fragmentation of source DNA
b. Amplification of source DNA
c. Detection and purification of clones
d. Joining of host DNA to a cloning vector
e. Incorporation of a cloning vector into the host cell

254. Nucleic acid probes are not only useful for searching for genes in the cloning host but also for searching for genes or gene fragments in patient specimens. Which one of the following statements is true of nucleic acid probes?

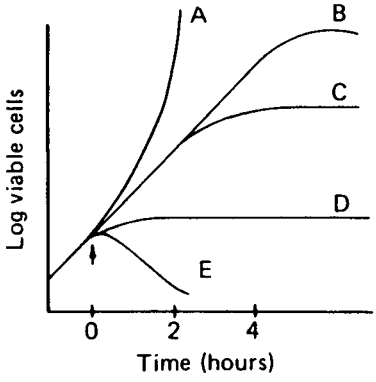
a. Only DNA can be used as a probe
b. Primers are labeled to allow detection, but probes are unlabeled
c. Nucleic acid probes are not as sensitive as traditional culture methods for detection of pathogenic microorganisms
d. Probes can be designed so that they can detect very specific pieces of a nucleic acid, for example, a penicillin-resistant gene
e. Probes may contain any part of the base sequence of the gene of interest

255. DNA from a host sample can be amplified by a process known as the polymerase chain reaction (PCR). Which of the following is required for PCR?

a. Knowledge of the genetic sequence to be amplified
b. An single nucleotide primer
c. An ultracentrifuge
d. A universal probe to detect the amplified product
e. A heat-sensitive DNA polymerase enzyme

Questions 256–259

The following five growth curves are lettered (A–E) corresponding to an expected growth curve if certain antibiotics were added to an exponentially growing culture of *E. coli*. The arrow indicates when antibiotics were added to the growing culture.



256. Chloramphenicol treatment would be expected to produce which one of the following growth curves?

a. A
b. B
c. C
d. D
e. E

257. Penicillin would be expected to produce which one of the following growth curves?

a. A
b. B
c. C
d. D
e. E

258. Sulfonamide would be expected to produce which one of the following growth curves?

a. A
b. B
c. C
d. D
e. E

259. If no antibiotics were added to the exponentially growing culture, which one of the following growth curves would result?

a. A
b. B
c. C
d. D
e. E

Questions 260–262

DNA can be transferred from one bacterium to another by a number of processes.

260. Uptake by a recipient cell of soluble DNA released from a donor cell is defined as

a. Conjugation
b. Recombination
c. Competence
d. Transformation
e. Transduction

261. Transfer of a donor chromosome fragment by a temperate bacterial virus is defined as

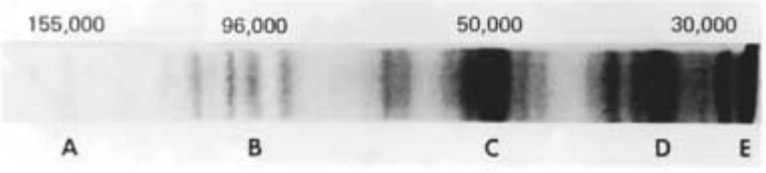
a. Conjugation
b. Recombination
c. Competence
d. Transformation
e. Transduction

262. Direct transfer of a plasmid between two bacteria is defined as

a. Conjugation
b. Recombination
c. Competence
d. Transformation
e. Transduction

Questions 263–266

A 7% sodium dodecyl sulfate polyacrylamide gel electrophoretogram of *E. coli* cell walls is shown below. The gel is labeled A–E.



263. The molecular weight of lactose permease is represented by

a. A
b. B
c. C
d. D
e. E

264. The molecular weight of *b* and *b*9 RNA polymerase is represented by

a. A
b. B
c. C
d. D
e. E

265. The molecular weight of flagellin, the major protein of bacterial flagella, is represented by

a. A
b. B
c. C
d. D
e. E

266. The molecular weight of the major cell-wall polypeptide is represented by

a. A
b. B
c. C
d. D
e. E

Questions 267–269

The diagram of freeze-fractured *E. coli* is labeled A–D, which represent various parts of the cell envelope.

267. The plasma membrane of *E. coli* is

a. Structure A
b. Structure B
c. Structure C
d. Structure D

268. The eutectic layer of *E. coli* is

a. Structure A
b. Structure B
c. Structure C
d. Structure D

269. The cell wall (lipoid layer) of *E. coli* is

a. Structure A
b. Structure B
c. Structure C
d. Structure D

270. A broad-spectrum antibiotic in the general class of thienamycins is

a. Piperacillin
b. Cefoperazone
c. Ceftriaxone
d. Ciprofloxacin
e. Imipenem

271. Third-generation cephalosporin with good activity against *Borrelia burgdorferi* is

a. Piperacillin
b. Cefoperazone
c. Ceftriaxone
d. Ciprofloxacin
e. Imipenem

272. Broad-spectrum penicillin with antipseudomonas activity is

a. Piperacillin
b. Cefoperazone
c. Ceftriaxone
d. Ciprofloxacin
e. Imipenem

273. Third-generation cephalosporin with primary activity against *Pseudomonas aeruginosa* is

a. Piperacillin
b. Cefoperazone
c. Ceftriaxone
d. Ciprofloxacin
e. Imipenem

274. Quinolone antibiotic with broad Gram-negative and Gram-positive activity is

a. Piperacillin
b. Cefoperazone
c. Ceftriaxone
d. Ciprofloxacin
e. Imipenem

275. Which one of the following antibiotics inhibits dihydrofolate reductase?

a. Penicillin
b. Amdinocillin
c. Amphotericin
d. Chloramphenicol
e. Trimethoprim

276. Which one of the following antibiotics binds to penicillin-binding protein-2 (PBP-2)?

a. Penicillin
b. Amdinocillin
c. Amphotericin
d. Chloramphenicol
e. Trimethoprim

277. Which one of the following antibiotics inhibits the final peptide bond between d-alanine and glycine?

a. Penicillin
b. Amdinocillin
c. Amphotericin
d. Chloramphenicol
e. Trimethoprim

278. Which one of the following antibiotics binds sterols and alters membrane permeability?

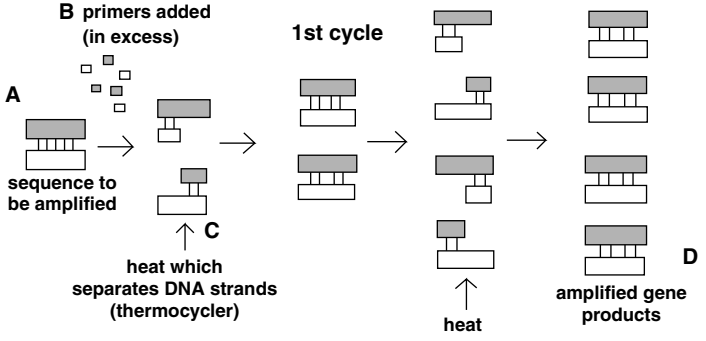
a. Penicillin
b. Amdinocillin
c. Amphotericin
d. Chloramphenicol
e. Trimethoprim

279. Which one of the following antibiotics attaches to 50S ribosome and inhibits peptidyl transferase?

a. Penicillin
b. Amdinocillin
c. Amphotericin
d. Chloramphenicol
e. Trimethoprim

Questions 280–284

The following diagram illustrates the amplification of DNA by the polymerase chain reaction (PCR). There are at least four points in the PCR process (A–D) that are critical to the reaction.



280. The Southern blot detection system for amplified PCR products fails to function. Which one of the following would be affected?

a. A
b. B
c. C
d. D

281. DNA does not hybridize with the primers. Which one of the following would be affected?

a. A
b. B
c. C
d. D

282. The laboratory observes a series of false-positive results. Which one of the following processes would you suspect to be faulty?

a. A
b. B
c. C
d. D

283. The DNA strands fail to reanneal. Which one of the following processes would you suspect to be faulty?

a. A
b. B
c. C
d. D

284. The laboratory observes a series of false-negative results. Which one of the following processes would you suspect to be faulty?

a. A
b. B
c. C
d. D

Questions 285–290

Bacteria or their components may be characterized by unique constituents or structures.

285. *Neisseria meningitidis,* group B, is characterized by

a. Repeating polysaccharide capsule of glucose and glucuronic acid
b. Outer-membrane proteins
c. γ-Glutamyl polypeptide
d. Sialic acid polymers
e. Hyaluronic acid

286. Group A streptococci are characterized by

a. Repeating polysaccharide capsule of glucose and glucuronic acid
b. Outer-membrane proteins
c. γ-Glutamyl polypeptide
d. Sialic acid polymers
e. Hyaluronic acid

287. Bacterial lipopolysaccharide (LPS) is characterized by

a. Phospholipid
b. Ribitol teichoic acid
c. Glycolipids (waxes)
d. Ketodeoxyoctonate
e. Repeating polysaccharide capsule of glucose and glucuronic acid

288. *Mycobacterium* cell walls are characterized by

a. Phospholipid
b. Ribitol teichoic acid
c. Glycolipids (waxes)
d. Ketodeoxyoctonate
e. Repeating polysaccharide capsule of glucose and glucuronic acid

289. *Bacillus anthracis* capsules consist of

a. Repeating polysaccharide capsule of glucose and glucuronic acid
b. Outer-membrane proteins
c. γ-Glutamyl polypeptide
d. Sialic acid polymers
e. Hyaluronic acid

290. *Streptococcus pneumoniae* are characterized by

a. Repeating polysaccharide capsule of glucose and glucuronic acid
b. Outer-membrane proteins
c. γ-Glutamyl polypeptide
d. Sialic acid polymers
e. Hyaluronic acid

Physiology and Molecular Microbiology

Answers

228. The answer is d. *(Levinson, p 57.)* The structural integrity of the β-lactam ring in penicillins is essential for their antimicrobial activity. Many resistant strains of staphylococci produce an enzyme, penicillinase, that cleaves the β-lactam ring at the carbon-nitrogen bond. Other organisms, including certain coliform bacteria, produce an amidase enzyme that inactivates penicillin by disrupting the bond between the radical and nitrogen in the free amino group (1 in the diagram).

229. The answer is b. *(Ryan, pp 26–27.)* Almost no important nutrients enter the bacterial cell through simple diffusion, an exception being carbon dioxide and oxygen. Some diffusion, however, is facilitated by specific protein carriers. Most transport, except simple diffusion, is energy-dependent, particularly in Gram-negative bacteria. Group translocation occurs in the absence of oxygen. For example, a simple carbohydrate such as glucose is phosphorylated enzymatically and is then transported into the cell.

230. The answer is e. *(Ryan, p 27.)* Siderophores such as aerobactin and enterobactin are chelators that trap iron Fe^{3+}. This Fe-chelator complex is actually transported inside the cell. Transferrin and lactoferrin are iron-binding proteins found in blood and milk. Ferric or iron oxide is rust and lipopolysaccharide (LPS) is a microbial cell-wall constituent.

231. The answer is a. *(Levinson, p 4.)* The periplasm is the space between the outer membrane and plasma membrane of bacteria. The periplasmic space in *Escherichia coli* has been shown to contain a number of proteins, sugars, amino acids, and inorganic ions. Ethylenediaminetetraacetic acid (EDTA) is a chelating agent that disrupts the cell walls of Gram-negative bacteria.

232–233. The answers are 232-a, 233-c. *(Ryan, pp 28–29.)* Oxygen, when it is metabolized, gives rise to hydrogen peroxide (H_2O_2) and super-

oxide-anion (O_2). Both of these byproducts are extremely toxic to cells. Peroxide is produced by many bacteria, particularly facultative anaerobes that use flavoprotein intermediates. H_2O_2 is degraded by peroxidases as illustrated in equation 2. Superoxide is detoxified by a critical enzyme known as superoxide dismutase. Such metabolism also results in H_2O_2 production (equation 1). *Peroxidase* and *catalase* are often used interchangeably to describe H_2O_2 reactions. However, in equation 2 when the H_2A reactant is another H_2O_2 molecule, the enzyme is known as *catalase*. If H_2A is another intermediate, then the enzyme is known as *peroxidase*.

234. The answer is a. *(Ryan, p 29.)* Superoxide dismutase is an enzyme found in both prokaryotic and eukaryotic cells that can survive in an environment of O_2. Lack of this enzyme as well as peroxidase and catalase insures that a bacterium will not grow in the presence of O_2. Absence of these enzymes is not related to virulence, although ability to survive in an O_2-rich atmosphere may impart certain benefits to the proliferation of bacteria in the human host.

235. The answer is c. *(Ryan, pp 25–29.)* 6-Phosphogluconic acid is a characteristic metabolic intermediate in the pentose-phosphate metabolic pathway. This pathway is used by heterolactic fermenters such as *Leuconostoc,* the organism responsible for the fermentation of cabbage in the production of sauerkraut. *Leuconostoc* is a Gram-positive bacterium with a dextran capsule.

236. The answer is b. *(Baron, pp 77–80.)* Adenosine triphosphate (ATP) is believed to be generated at three reaction points in the electron transport chain: the reductions of flavoprotein, cytochrome b, and cytochrome c. This phenomenon, demonstrated in experiments with mammalian mitochondria, can be expressed in terms of the relationship between the moles of ATP generated for each atom of oxygen consumed—the P/O ratio. In mammalian cells, the P/O ratio is 3; that is, there are three segments in the electron transfer chain in which there is a relatively large free energy drop. In bacteria, however, there appears to be only one or two of these segments. Loss of these phosphorylation sites as well as reactions that bypass these sites of ATP synthesis account for the lower P/O ratio in bacteria. Some bacteria, such as *Mycobacterium phlei,* have P/O ratios of 3.

237. The answer is a. *(Levinson, pp 5–7.)* Bacteria may shift rapidly between the fimbriated (fim +) and the nonfimbriated (fim –) states. Fimbriae function as adhesions to specific surfaces and consequently play a major role in pathogenesis. Lack of fimbriae prevents colonization of the mucosal surface by the bacterium.

238. The answer is c. *(Levinson, pp 109–114.)* Region 1 (the O-antigenic side chain of lipopolysaccharide) is responsible for the many serotypes of *Salmonella.* A mutant of *Salmonella* deficient in region 1 is not identified as a "newport," at least by virtue of its somatic antigen; biochemical identification of this mutant would be *S. enteritidis.* Loss of region 1 does not affect genus and species classification of *Salmonella.* Recently, however, it has been recommended that *Salmonella* be referred to by genus and serovar, that is, *Salmonella newport* or *Salmonella* serovar newport.

239. The answer is e. *(Ryan, pp 31–33.)* Penicillin-binding proteins (PBPs) combine with penicillin and inhibit the final cross-linking of peptidoglycan in the cell wall. All of the other choices are involved in polymerization processes. Examples of polymerization include the cell membrane (bactoprenol) and synthesis of DNA and RNA.

240. The answer is b. *(Levinson, pp 6, 12–13.)* Dipicolinic acid, formed in the synthesis of diaminopimelate (DAP), is a prominent component of bacterial spores but is not found in vegetative cells or eukaryotic appendages or fimbrial structures. The calcium salt of dipicolinic acid apparently plays an important role in stabilizing spore proteins, but its mechanism of action is unknown. Dipicolinic acid synthetase is an enzyme unique to bacterial spores.

241–243. The answers are 241-a, 242-b, 243-c. *(Ryan, pp 34–36.)* Bacterial growth curves are multiphasic. The lag phase is characterized by lack of growth but not necessarily metabolic activity. The bacteria are "adjusting" to their new environment. Depending on the bacteria, the temperature, nutrients, and pH, the microorganisms start dividing after a few hours and grow logarithmically for 12 to 18 h. Toxins accumulate in the medium and nutrients become limiting. Oxygen and CO_2 are usually not limiting, as the gases freely diffuse into the growing culture. When death and growth of cells are equal, the stationary phase occurs. The death phase

is characterized by a death rate that is more rapid than the growth rate. An antibiotic which inhibits protein synthesis would be optimally active in a rapidly dividing culture where proteins are being rapidly synthesized, that is, the logarithmic phase. Bacteria introduced into the human host may undergo similar phases of growth. However, other factors such as host defenses play a major role in limiting logarithmic growth as does accumulation of toxic byproducts as might occur in a closed-space infection such as an abscess.

244. The answer is b. *(Levinson, pp 54–66.)* Ideally, antibiotics should attack a microbial structure or function not found in human cells. Except for mitomycin, all the antibiotics listed in the question interfere with cell-wall synthesis in bacteria. Mitomycin inhibits DNA synthesis in both mammalian and microbial systems; viral DNA synthesis, however, is relatively resistant to mitomycin.

245. The answer is a. *(Davis, pp 30–43.)* Freeze-etching involves the freezing of cells at very low temperatures in a block of ice. The ice block is split with a knife, and ice crystals are sublimed (etched) from one of the newly exposed faces. The line of fracture often passes through a natural cleavage plane—in the illustration presented in the question, for example, the inner and outer faces of the cell membrane of an *E. coli*. Freeze-etching does not produce the troublesome artifacts introduced during the fixation and drying of specimens.

246. The answer is c. *(Levinson, pp 4–7.)* *E. coli* has two major porins, OMP C and OMP E (OMP is outer-membrane protein). A porin is a protein trimer with each subunit containing a pore with a diameter of 1 nm. Porins function in outer-membrane (OM) permeability. While porins are known to permit the transfer of small molecules across the OM, specific porins may also influence the diffusion of layer molecules. Depending on charge, porins may also repel certain molecules, such as bile salts found in the intestinal environment.

247. The answer is c. *(Levinson, pp 147–148.)* The serologic diagnosis of Lyme disease is fraught with difficulty. Enzyme immunoassay (EIA) may be insensitive in the early stages of disease and may lack specificity in advanced stages. Western blot analysis of antibody is the confirmatory test

for Lyme disease, but it, too, is not 100% sensitive and specific. The Western blot test detects antibodies to proteins and glycoproteins of *Borrelia burgdorferi*. Not all of these proteins are specific for the organism. For example, antibodies to Gp66 may reflect a cross-reaction, as many Gram-negative bacteria have similar glycoproteins. For this reason, a Western blot showing only antibodies to Gp66 is thought to be a nonspecific immune response.

248. The answer is b. *(Ryan, pp 243–245.)* DNA polymerase isolated from the hot springs thermophilic bacterium named *Thermus aquaticus* is essential for the polymerase chain reaction (PCR) process because of its stability at high temperatures (95°C). While the *E. coli* enzyme can be used, the enzyme itself becomes denatured, fewer cycles are possible, and nonspecific reactions occur because of hybridization of primers to nontarget DNA. The use of Taq polymerase allows DNA copying at 72°C rather than 37°C, which further reduces nonspecific hybridization.

249–251. The answers are 249-d, 250-e, 251-a. *(Ryan, pp 242–245.)* The polymerase chain reaction (PCR) has revolutionized the detection of infectious microorganisms, particularly those that are difficult to grow. While physicians during their normal practice will usually not be required to design a PCR test, they should know some of the design elements of PCR so that they might better understand the results from these widely used tests.

One of the major problems of PCR in the past was contamination from extraneous nucleic acid. There are several ways to prevent contamination and the resulting falsely positive results. They include the use of separate laboratories, hoods, gloves, and surface disinfectants. The most effective method, however, is the use of internal sterilizing agents such as uracil N-glycosyls (UNG). These agents cross-link extraneous DNA so that the product cannot be amplified. Primers now can be purchased from a catalogue and their sequence obtained online. Primers are easily synthesized, must be complementary to sequences on the bacterial chromosome, and when coupled to such sequences must promote replication. The specificity of PCR is a function of choosing a primer pair that is unique to the organism that you wish to detect. The PCR process is best explained by the "needle in the haystack" analogy. One needle in a haystack is difficult to find. However, if one needle becomes a million needles, then detection is easy. The same is

true for nucleic acids. The amplicons (amplified nucleic acids) can be detected by a number of methods because they are so plentiful. These methods include specific staining with ethidium bromide of a gel containing these amplicons and Southern blotting of the amplicons "tags" them so that they can be seen on photographic film. Amplicons are also bound to solid phases and detected with labeled enzymes or an instrument that reads a fluorescent tag. Microscopy is not used.

252. The answer is a. *(Baron, pp 48–49.)* The organisms illustrated in the question are spheroplasts of *E. coli*. Lysozyme clears the b-1-4-glycosidic bond between *N*-acetylmuramic acid and *N*-acetylglucosamine. Spheroplasts are bacteria with cell walls that have been partially removed by the action of lysozyme or penicillin. Ordinarily, with disintegration of the walls, the cells undergo lysis; however, in a hypertonic medium, the cells persist and assume a spherical configuration. Endospores are formed by Gram-positive bacteria in the genera *Bacillus* and *Clostridium*. It has also been shown that for *E. coli* and other Gram-negative rods, exposure to minimal concentrations of antibiotics does not rupture the cell wall but promotes elongation of the cell by inhibiting the division cycle.

253. The answer is a. *(Ryan, pp 65–66.)* Gene cloning is a basic step in virtually every genetic-engineering process. First, the source DNA is isolated and cut into small pieces and then attached to a cloning vector with DNA ligase. The cloning vectors are inserted into the host organism (usually a bacterium), and then the cloned DNA is isolated, identified, and purified. Amplification of source DNA is not a necessary step.

254. The answer is d. *(Ryan, pp 243–246.)* Nucleic acid probes, either DNA or RNA, are commonly used in clinical and research microbiology laboratories. These complementary pieces of nucleic acid bind to genes or gene parts of interest and are detected by their label, which may be either radioactive or nonradioactive. Probes, in general, are more sensitive than traditional growth-dependent methods, particularly for those microorganisms that either cannot be cultured or grow very slowly.

255. The answer is a. *(Ryan, pp 243–246.)* PCR is a widely used tool for amplification of small pieces of nucleic acid present in minute quantities. Once the sequence to be amplified is known, a specific primer is added.

The temperature is alternately raised and lowered up to 45 to 50 times in the presence of a heat-resistant DNA polymerase from *T. aquaticus*. The amplified gene product is then detected by one of a number of techniques.

256–259. The answers are 256-d, 257-e, 258-c, 259-b. *(Levinson, pp 54–56.)* Penicillin causes lysis of growing bacterial cells. Its antimicrobial effect stems from impairment of cell-wall synthesis. Because penicillin is bactericidal, the number of viable cells should fall immediately after introduction of the drug into the medium.

Both chloramphenicol and sulfonamides are bacteriostatic—that is, they retard cell growth without causing cell death. Chloramphenicol causes an immediate, reversible, bacteriostatic inhibition of protein synthesis. Sulfonamides, on the other hand, compete with para-aminobenzoic acid in the synthesis of folate; intracellular stores of folate are depleted gradually as the cells continue to grow.

The number of viable cells in a culture eventually will level off even if no antibiotic is added to the environment. A key factor in this phenomenon is the limited availability of substrate.

260–262. The answers are 260-d, 261-e, 262-a. *(Ryan, pp 50–52.)* Transformation, transduction, and conjugation are critical processes in which DNA is transferred from one bacterium to another. Transformation, the passage of high-molecular-weight DNA from one bacterium to another, was first observed in pneumococci. Later studies have shown that, at least in *Streptococcus pneumoniae,* double-stranded DNA is "nicked" by a membrane-bound endonuclease, initiating DNA entry into the host cell. One of the nicked DNA strands is digested, and the other is integrated into the host genome.

In conjugation, too, DNA is passed from one bacterium to another. However, instead of the transfer of soluble DNA, a small loop of DNA, called a *plasmid,* is passed between cells. Examples of plasmids are the sex factors and the resistance (R) factors.

Transduction, which can affect many bacteria, is a process in which a fragment of donor chromosome is carried to a recipient cell by a temperate virus (bacteriophage). In generalized transduction, the phage virus can carry any segment of the donor chromosome; in restricted transduction, the phage carries only those chromosomal segments immediately adjacent to the site of prophage attachment.

263–266. The answers are 263-d, 264-a, 265-c, 266-c. *(Davis, p 138.)* Gel electrophoresis provides a rapid method for identifying bacterial proteins and estimating molecular weights. A gel can be made of a number of substances, including starch, agar, and polyacrylamide. Starch gel has high separating power because the fine gel pores act as a molecular sieve. Agar gel is easier to prepare than starch; separation of proteins is accomplished in 30 to 60 min. Polyacrylamide gel also separates on the principle of the molecular sieve. It is chemically inert and electrically neutral. The biggest disadvantage of polyacrylamide is that its separating powers are so good that protein patterns, or patterns of other heterogeneous substances, may be too complex to interpret. In the electrophoretogram presented in the question, band A represents RNA polymerases (molecular weight 155,000), band C represents both flagellin and the major cell-wall protein (50,000), and band D represents lactose permease (30,000). Band E is the dye front.

267–269. The answers are 267-a, 268-c, 269-d. *(Davis, pp 30–43.)* Freeze-fracture is a process in which cells are frozen and then cleaved with a knife. Ice is sublimed from the cleaved surface, and underlying structures are laid bare. The fracture lines in the ice often pass through cells along natural lines of cleavage and reveal internal surfaces through shadowing on microscopy. Natural bacterial cell planes of cleavage occur between the peptidoglycan layer and the plasma membrane and between the inner and outer faces of the membrane. In the freeze-fracture photograph presented in the question, the concave fractures from the inside of the envelope out include the plasma membrane (A), peptidoglycan layer (B), and the lipopolysaccharide layer (D). Structure C is the eutectic layer.

270–274. The answers are 270-e, 271-c, 272-a, 273-b, 274-d. *(Howard, pp 145–196.)* Many new antibiotics have become available during the past few years. Although expensive, these antibiotics generally have a broader spectrum of effectiveness than the ones they are intended to replace. Resistance to these newly introduced agents may be a problem that will minimize their effects on the treatment of infectious disease. While most are labeled *broad spectrum,* each appears to be characteristically more effective against some organisms than others.

Ceftriaxone is a new-generation cephalosporin. It is administered once a day either intravenously or intramuscularly. While ceftriaxone is used

against a wide variety of Gram-negative rods, it has found special use in the treatment of Lyme disease. It is now claimed to be the most effective antibiotic for borreliosis.

275–279. The answers are 275-e, 276-b, 277-a, 278-c, 279-d. *(Levinson, pp 54–56.)* The antibiotics in these questions have significantly different modes of action. Recent evidence suggests that while penicillin inhibits the final cross-linking of the cell wall, it also binds to penicillin-binding proteins and inhibits certain key enzymes involved in cell-wall synthesis. The mechanism is complex. Amdinocillin, although classified as a penicillin, selectively binds to penicillin-binding protein-2 (PBP-2). Binding to PBP-2 results in aberrant cell-wall elongation and spherical forms, seen when *E. coli,* for example, is exposed to mecillinam.

Because amphotericin binds to sterols (such as cholesterol) in the cell membrane, its range of activity is predictable; that is, it is effective against microorganisms that contain sterol in the cell membrane (such as molds, yeasts, and certain amebae). These polyene antibiotics cause reorientation of sterols in the membrane, and membrane structure is altered to the extent that permeability is affected. If sterol synthesis is blocked in fungi, then amphotericin is not effective. This occurs when fungi are exposed to miconazole, another antifungal antibiotic.

Chloramphenicol is a bacteriostatic antibiotic. Its action does not kill the cell but only inhibits it. If chloramphenicol is removed from the culture, then protein synthesis is reinitiated. Bacterial ribosomes are spherical particles with a molecular weight of 3 3 106. Protein synthesis takes place on the ribosome by a complex process involving various ribosomal subunits, tRNA, and nRNA. Chloramphenicol, in contrast to the aminoglycosides and tetracycline, attaches to the 50S ribosome subunit. The enzyme peptidyl transferase, found in the 50S subunit, is inhibited. Removal of the inhibition—in this case, chloramphenicol—results in full activity of the enzyme.

Trimethoprim (TMP), a diaminopyrimidine, is a folic acid antagonist. Although TMP is commonly used in combination with sulfa drugs, its mode of action is distinct. TMP is structurally similar to the pteridine portion of dihydrofolate and prevents the conversion of folic acid to tetrahydrofolic acid by inhibition of dihydrofolate reductase. Fortunately, this enzyme in humans is relatively insensitive to TMP.

280–284. The answers are 280-d, 281-c, 282-a, 283-c, 284-b. *(Howard, pp 136, 773.)* The process of PCR is complicated and its steps are interrelated. A number of steps in the process can markedly affect the results of clinical testing. For example, the detection of amplified products is essential in order to determine whether target nucleic acid was present in the specimen. Product can be detected by staining of the gel that separates the products, Southern blot (a radioactive procedure), or an ELISA-like capture method. A failure of this production step prevents detection of product.

One of the essential parts of the PCR process is the thermal cycling of the reaction. If the reaction is not heated, primer DNA will not hybridize with the target sequences. Nor will the strands reanneal if the mixture is not cooled. Failure of the thermocycler could cause such a problem.

False-positive results are usually due to contamination of the reaction by foreign DNA. In such a case, the foreign DNA sequences are amplified even if the target sequences are not present.

There are a number of reasons why PCR would be falsely negative, but a prime reason is failure to choose the right primer sets. Suboptimum detection of amplified products is another. Ethidium bromide staining of the PCR gel is less sensitive than detection of the products by Southern blot.

285–290. The answers are 285-d, 286-e, 287-d, 288-c, 289-c, 290-a. *(Baron, pp 38–48.)* Bacteria have a variety of components; some are unique to certain genera and species, others are characteristic of all bacteria. All bacteria have peptidoglycan in their cell walls, although the peptidoglycan layer is much thinner in Gram-negative than Gram-positive bacteria. In Gram-positive bacteria, teichoic acids, polysaccharides, and peptidoglycolipids are covalently attached to the peptidoglycans. While *Mycobacterium* also has peptidoglycan, up to 40% of the cell wall may be a waxy glycolipid that is responsible for the "acid fastness" of *Mycobacterium* and *Nocardia,* an aerobic actinomycete. Bacterial lipopolysaccharide (LPS), also known as *endotoxin,* is found in only Gram-negative bacteria. Not only is it a toxic macromolecule, but it also imparts serologic specificity to some Gram-negative bacteria such as *Salmonella* and *E. coli.*

Capsules are found in both Gram-positive and Gram-negative bacteria. With the exception of those found in *Bacteroides fragilis,* capsules are not in and of themselves toxic but rather are antiphagocytic and are

immunologic (or serologic) determinants. Some examples of capsular components are the following:

1. Sialic acid polymers are found in group B *Neisseria meningitidis*. This identical polymer is also found in *E. coli* K1.
2. Group A streptococci in the early stages of growth have hyaluronic acid capsules. The capsule, however, is rapidly destroyed by the organism's own hyaluronidase.
3. *Bacillus anthracis,* the causative agent of anthrax, is the only bacterium to possess a polypeptide capsule that is a polymer of glutamic acid.
4. *S. pneumoniae* type 3 has a repeating polysaccharide capsule of glucose and glucuronic acid.

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Rickettsiae, Chlamydiae, and Mycoplasmas

Questions

DIRECTIONS: Each question below contains five suggested responses. Select the **one best** response to each question.

291. Mycoplasmas differ from chlamydiae in that they are

a. Susceptible to penicillin
b. Able to grow on artificial cell-free media
c. Able to cause urinary tract infection
d. Able to stain well with Gram's stain
e. Able to cause disease in humans

292. Q fever

a. Is an illness confined to the upper respiratory tract
b. Has an incubation period of 4 to 6 weeks
c. Is most commonly found in tropical regions
d. Is transmitted by the bite of an arthropod
e. Is an acute febrile illness caused by *Coxiella burnetii*

293. Rickettsiae, which include the spotted fevers, Q fever, typhus, and scrub typhus, are

a. Obligate intracellular parasites
b. Stable outside the host cell
c. Easily stained (Gram-negative) with a Gram stain
d. Maintained in nature with humans as the mammalian reservoir
e. The cause of infections in which a rash is always present

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294. A man with chills, fever, and headache is thought to have "atypical" pneumonia. History reveals that he raises chickens and that approximately 2 weeks ago he lost a large number of them to an undiagnosed disease. The most likely diagnosis of this man's condition is

a. Anthrax
b. Q fever
c. Relapsing fever
d. Leptospirosis
e. Ornithosis (psittacosis)

295. An ill patient denied being bitten by insects. However, he had spent some time in a milking barn and indicated that it was dusty. Of the following rickettsial diseases, which one has he most likely contracted?

a. Scrub typhus
b. Rickettsialpox
c. Brill-Zinsser disease
d. Q fever
e. Rocky Mountain spotted fever (RMSF)

296. Which of the following mycoplasmas has been implicated as a cause of nongonococcal urethritis (NGU)?

a. *Mycoplasma hominis*
b. *M. pneumoniae*
c. *M. fermentans*
d. *M. mycoides*
e. *Ureaplasma urealyticum*

297. Which of the following statements best describes human monocytic ehrlichiosis (HME)?

a. The HME agent grows on artificial media
b. It is a fatal disease transmitted by the bite of a dog
c. Clinical diagnosis is based on the presence of erythema migrans (EM)
d. Symptoms include vomiting and paralysis
e. Diagnosis is usually made serologically but morulae may be seen in the cytoplasm of monocytes

298. Lymphogranuloma venereum (LGV) is a venereal disease caused by serotype L1, L2, or L3 of *Chlamydia trachomatis*. The differential diagnosis should include which of the following?

a. Psittacosis
b. Chancroid
c. Shingles
d. Babesiosis
e. Mononucleosis

299. An inhibitor of ATP synthesis would be expected to retard most severely the penetration of the host cell by which of the following organisms?

a. *Chlamydia psittaci*
b. *C. trachomatis*
c. *U. urealyticum*
d. *Rickettsia rickettsii*
e. *M. pneumoniae*

300. *C. trachomatis* can be distinguished from *C. psittaci* by which of the following criteria?

a. *C. trachomatis* is sensitive to sulfonamides
b. *C. trachomatis* has a different lipopolysaccharide antigen
c. *C. trachomatis* can be stained with Giemsa
d. *C. psittaci* is an obligate prokaryotic parasite
e. *C. psittaci* forms inclusions that contain glycogen

301. Chlamydiae have an unusual three-stage cycle of development. The correct sequence of these events is

a. Penetration of the host cell, synthesis of elementary body progeny, development of an initial body
b. Penetration of the host cell, development of an initial body, synthesis of elementary body progeny
c. Development of an initial body, synthesis of elementary body progeny, penetration of the host cell
d. Synthesis of elementary body progeny, development of an initial body, penetration of the host cell
e. Synthesis of elementary body progeny, penetration of the host cell, development of an initial body

302. Rickettsiae are Gram-negative bacteria that cause a wide range of diseases. The agent of Rocky Mountain spotted fever (RMSF) is best characterized by the statement that it

a. Grows on 7% sheep blood agar
b. Has an "atypical" Gram-negative cell wall
c. Is energy-deficient and cannot phosphorylate glucose
d. Is normal flora of the mosquito gut
e. Is susceptible to penicillin

303. Human granulocytic ehrlichiosis (HGE) is a disease transmitted to humans by the bite of a tick, *Ixodes scapularis*. Which of the following statements about HGE is most correct?

a. Clinical diagnosis is based on the presence of erythema migrans
b. HGE is a self-limiting disease
c. HGE is caused by *Ehrlichia chaffeensis*
d. The causative organism can be grown on ordinary laboratory media
e. HGE is characterized by an acute onset of fever, severe headache, and influenza-like symptoms

304. The "spotted fever" group of rickettsial diseases is caused by a variety of rickettsial species. While not critical for treatment of disease, the speciation of these organisms is essential for epidemiologic studies. Of the following rickettsiae, which one is found in the United States and is a member of the spotted fever group?

a. *Rickettsia sibirica*
b. *R. conorii*
c. *R. akari*
d. *R. prowazekii*
e. *R. australis*

305. A 36-year-old man presents at his physician's office complaining of fever and headache. On examination, he had leukopenia and increased liver enzymes, and inclusion bodies were seen in his monocytes. History revealed that he was an outdoorsman and remembered removing a tick from his leg. Which of the following diseases is most likely causing the symptoms described?

a. Lyme disease
b. Ehrlichiosis
c. Rocky Mountain spotted fever
d. Q fever
e. Tularemia (*Francisella tularensis*)

306. Typhus, spotted fever, and scrub typhus share which of the following manifestations of disease?

a. Short incubation period (<48 h)
b. Fever, rash, and rickettsemia
c. Common vector
d. Similar geographic distribution
e. Arthritis

307. *C. trachomatis* is a well-known cause of venereal disease. This organism is also implicated in which of the following?

a. Classic trachoma infection
b. Sexually transmitted cardiac disease in adults
c. Perinatal retinitis
d. Middle-ear infection in young children
e. Urinary tract infection in children

308. Which one of the following statements best characterizes lymphogranuloma venereum (LGV)?

a. The causative agent is *C. trachomatis*
b. In the United States, it is more common among women
c. It is most common in temperate regions
d. Penicillin is effective in early treatment
e. The disease (LGV) does not become chronic

309. Trachoma is one of the leading causes of blindness. Which of the following best typifies the disease?

a. It is caused by *C. trachomatis*
b. It is best treated with systemic cephalosporins and ophthalmic tetracycline
c. It affects 400 million people in the Pacific Rim
d. It is a form of chronic uveitis
e. Chlamydial eye infection is a major veterinary problem

310. Chlamydiae are small Gram-negative rods once thought to be viruses. Which of the following best characterizes chlamydiae as distinct from viruses?

a. Independent synthesis of proteins
b. Susceptibility to antimicrobial agents
c. Intracellular reproduction
d. Synthesis of ATP
e. Cannot visualize with light microscope

311. *Chlamydia pneumoniae,* sometimes known as *Chlamydia* "TWAR," is the most recent *Chlamydia* species to be associated with human disease. Which one of the following statements best describes *C. pneumoniae?*

a. *C. pneumoniae* infections are generally severe
b. *C. pneumoniae* infections are uncommon—up to 10% of adults may show specific antibody
c. Nonpsittacine birds are reservoirs of *C. pneumoniae*
d. Infections with *C. pneumoniae* usually arise from bacterial overgrowth in the colon
e. *C. pneumoniae* has been associated with myocardial infarction

Questions 312–315

Members of the family of *Mycoplasma* have a variety of clinical and epidemiological features.

312. Which one of the following organisms causes primary atypical pneumonia in humans?

a. *M. hominis*
b. *M. orale*
c. *M. pneumoniae*
d. *M. fermentans*
e. *U. urealyticum*

313. Which one of the following organisms is associated with nongonococcal urethritis in humans?

a. *M. hominis*
b. *M. orale*
c. *M. pneumoniae*
d. *M. fermentans*
e. *U. urealyticum*

314. Which one of the following organisms normally inhabits the healthy human oral cavity?

a. *M. hominis*
b. *M. orale*
c. *M. pneumoniae*
d. *M. fermentans*
e. *U. urealyticum*

315. Which one of the following organisms normally inhabits the female genital tract but may cause acute respiratory illness?

a. *M. hominis*
b. *M. orale*
c. *M. pneumoniae*
d. *M. fermentans*
e. *U. urealyticum*

Questions 316–320

The following group of organisms is characterized as rather difficult to cultivate with some interesting molecular and physiologic similarities.

Bartonella (Rochalimaea) henselae
E. chaffeensis
C. trachomatis
R. rickettsii
C. burnetii

316. The causative agent of lymphogranuloma venereum is

a. *B. (Rochalimaea) henselae*
b. *E. chaffeensis*
c. *C. trachomatis*
d. *R. rickettsii*
e. *C. burnetii*

317. Which one of the following is transmitted by the bite of a hard *Ixodes* tick?

a. *B.* (*Rochalimaea*) *henselae*
b. *E. chaffeensis*
c. *C. trachomatis*
d. *R. rickettsii*
e. *C. burnetii*

318. Which of the following microorganisms is the causative agent of cat-scratch fever?

a. *B.* (*Rochalimaea*) *henselae*
b. *E. chaffeensis*
c. *C. trachomatis*
d. *R. rickettsii*
e. *C. burnetii*

319. Which of the following is a Gram-negative rickettsia with tropism for mononuclear cells and causes Q fever?

a. *B.* (*Rochalimaea*) *henselae*
b. *E. chaffeensis*
c. *C. trachomatis*
d. *R. rickettsii*
e. *C. burnetii*

320. Which of the following is the causative agent of Rocky Mountain spotted fever?

a. *B.* (*Rochalimaea*) *henselae*
b. *E. chaffeensis*
c. *C. trachomatis*
d. *R. rickettsii*
e. *C. burnetii*

Rickettsiae, Chlamydiae, and Mycoplasmas

Answers

291. The answer is b. *(Levinson, pp 143–144.)* Mycoplasmas lack a rigid cell wall and are bound by a triple-layer unit membrane. For this reason, they are completely resistant to the action of penicillins. Unlike the chlamydiae, they can replicate in cell-free media.

292. The answer is e. *(Levinson, pp 153–155.)* Q fever is an acute, flu-like illness caused by *Coxiella burnetii.* It is the one rickettsial disease not transmitted by the bite of a tick. *C. burnetii* is found in high concentrations in the urine, feces, placental tissue/amniotic fluid of cattle, goats, and sheep. Transmission to humans is by aerosol inhalation of those specimens.

293. The answer is a. *(Levinson, pp 153–155.)* Rickettsiae are obligate intracellular parasites who depend on host cells for their phosphorylated energy compounds. The significant rickettsial diseases in North America include Rocky Mountain spotted fever (*Rickettsia rickettsii*), Q fever (*C. burnetii*), and typhus (*R. prowazekii, R. typhi*). Laboratory diagnosis of rickettsial disease is based on serologic analysis rather than isolation of the organism.

294. The answer is e. *(Levinson, pp 150–152.)* Ornithosis (psittacosis) is caused by *Chlamydia psittaci.* Humans usually contract the disease from infected birds kept as pets or from infected poultry, including poultry in dressing plants. Although ornithosis may be asymptomatic in humans, severe pneumonia can develop. Fortunately, the disease is cured easily with tetracycline.

295. The answer is d. *(Levinson, pp 153–155.)* Most rickettsial diseases are transmitted to humans by way of arthropod vectors. The only exception is Q fever, which is caused by *C. burnetii.* This organism is transmitted by inhalation of contaminated dust and aerosols or by ingestion of contaminated milk.

296. The answer is e. *(Levinson, pp 143–144.) Ureaplasma urealyticum* has been associated with nongonococcal urethritis (NGU) as well as infertility. *Mycoplasma pneumoniae* is the etiologic agent of primary atypical pneumonia. *M. hominis,* although isolated from up to 30% of patients with NGU, has yet to be implicated as a cause of that disease. *M. fermentans* has on rare occasions been isolated from the oropharynx and genital tract. *M. mycoides* causes bovine pleuropneumonia.

297. The answer is e. *(Levinson, p 158.)* Human monocytic ehrlichiosis (HME), caused by the bite of the tick *Amblyomma americanum* infected with *Ehrlichia chaffeensis,* causes an illness not unlike RMSF, except a rash usually does not occur. Diagnosis is usually made serologically and treatment of choice is tetracycline. Symptoms include high fever, severe headache, and myalgias.

298. The answer is b. *(Levinson, pp 150–152.)* The differential diagnosis of lymphogranuloma venereum (LGV) includes syphilis, genital herpes, and chancroid. Several clinical tests can be used to rule out syphilis and genital herpes. These include a positive dark-field examination as well as positive serologic findings for syphilis and the demonstration of herpes simplex virus by cytology or culture. *Haemophilus ducreyi* can usually be isolated from the ulcer in chancroid.

299. The answer is d. *(Levinson, pp 153–155.)* Of the organisms listed in the question, only *R. rickettsii* penetrates host cells by an active process requiring the expenditure of energy (i.e., ATP). Chlamydiae have a complex growth cycle, which is obligately intracellular. Although the precise mode of penetration is not known, it is likely that a vesicle is formed around the chlamydiae, which then are taken into the cell by a mechanism similar to phagocytosis; chlamydiae do not synthesize ATP. Mycoplasma species are free-living bacteria that do not actively penetrate cells.

300. The answer is a. *(Levinson, pp 150–152.)* The chlamydiae are obligate prokaryotic parasites of eukaryotic cells. For many years, they were considered to be viruses but are now considered to be bacteria. The two species, *C. trachomatis* and *C. psittaci,* can be distinguished by two criteria: the susceptibility of *C. trachomatis* to sulfonamides and its ability to form inclusions containing glycogen.

301. The answer is b. *(Levinson, pp 150–152.)* The developmental cycle of chlamydiae begins with the elementary body attaching to and then penetrating the host cell. The elementary body, now in a vacuole bounded by host-cell membrane, becomes an initial body. Within about 12 h, the initial body has divided to form many small elementary particles encased within an inclusion body in the cytoplasm; these progeny are liberated by host-cell rupture.

302. The answer is c. *(Baron, pp 489–497.)* Rickettsiae are energy-deficient parasites that cannot use glucose as an energy source without its being phosphorylated. This is thought to be due to a transport defect rather than to a leaky membrane or atypical cell wall. With the exception of *Rochalimaea* (*Bartonella*) *quintana,* the agent of trench fever, rickettsiae cannot be cultivated on artificial media. The usual vector for disease is the tick.

303. The answer is e. *(Baron, pp 487–488.)* HGE is caused by the bite of *Ixodes scapularis* infected with an as yet unnamed *Ehrlichia.* The agent is nearly identical to *E. equi.* A rash rarely occurs and erythema migrans (EM) does not occur.

304. The answer is c. *(Howard, pp 856–857.)* The primary cause of Rocky Mountain spotted fever (RMSF) is *R. rickettsii,* although rickettsialpox is caused by *R. akari,* the only other member of the spotted fever group that resides in the United States. *R. sibirica* is responsible for tick typhus in China; *R. australis* causes typhus in Australia, as the name signifies; and *R. conorii* causes European and African rickettsioses. *R. prowazekii* is not a member of the spotted fever group; it causes epidemic typhus.

305. The answer is b. *(Levinson, pp 147–148, 153–155.)* All the listed diseases except Q fever are tick-borne. The rickettsia *C. burnetii* causes Q fever, and humans are usually infected by aerosol of a sporelike form shed in milk, urine, feces, or placenta of infected sheep, cattle, or goats. Lyme disease is caused by a spirochete, *Borrelia burgdorferi,* and produces the characteristic lesion erythema chronicum migrans (ECM). The etiologic agent of Rocky Mountain spotted fever is *R. rickettsia.* It usually produces a rash that begins in the extremities and then involves the trunk. Two human forms of ehrlichiosis can occur: human monocytic ehrlichiosis (HME), caused by *E. chaffeensis;* and human granulocytic ehrlichiosis

(HGE), caused by an as yet unnamed *Ehrlichia.* Ehrlichiosis was previously recognized only as a veterinary pathogen. HME infection is transmitted by the brown dog tick and *A. americanum.* HGE infection is transmitted by *I. scapularis,* the same tick that transmits Lyme disease. Both infections cause fever and leukopenia. A rash rarely occurs. *E. chaffeensis* infects monocytes, and HGE infects granulocytes; both organisms produce inclusion bodies called *morulae. Francisella tularensis* is a small, Gram-negative, nonmotile coccobacillus. Humans most commonly acquire the organism after contact with tissues or body fluid of an infected mammal or the bite of an infected tick.

306. The answer is b. *(Levinson, pp 153–155.)* Typhus, spotted fever, and scrub typhus are all caused by rickettsiae (*R. prowazekii, R. rickettsii,* and *R. tsutsugamushi,* respectively). Clinically, the diseases have several similarities. Each has an incubation period of 1 to 2 weeks followed by a febrile period, which usually includes a rash. During the febrile period, rickettsiae can be found in the patient's blood and there is disseminated focal vasculitis of small blood vessels. The geographic area associated with these diseases is usually different. Scrub typhus is usually found in Japan, Southeast Asia, and the Pacific, while spotted fever is usually found in the Western hemisphere. Typhus has a worldwide incidence.

307. The answer is a. *(Levinson, pp 150–152.)* Trachoma has been the greatest single cause of blindness in the world. *Chlamydia trachomatis* is the most common cause of sexually transmitted disease in the United States and is also responsible for the majority of cases of infant conjunctivitis and infant pneumonia.

308. The answer is a. *(Levinson, pp 150–152.)* LGV is a sexually transmitted disease caused by *C. trachomatis* of immunotypes L1, L2, and L3. It is more commonly found in tropical climates. In the United States, the sex ratio is reported to be 3.4 males to 1 female. Tetracycline has been successful in treating this disease in the early stages; however, late stages usually require surgery.

309. The answer is a. *(Levinson, pp 150–152.)* Trachoma is the most common cause worldwide of blindness. It is a chronic keratoconjunctivitis

that affects about 400 million people and can be treated with sulfonamides and tetracycline. Relapse of trachoma is common.

310. The answer is a. *(Levinson, pp 150–152.)* Although both chlamydiae and viruses are obligate, intracellular parasites and depend on the host cell for ATP and phosphorylated intermediates, they differ in many respects. Unlike viruses, chlamydiae synthesize proteins and reproduce by fission. Chlamydiae are readily seen under the light microscope and possess bacteria-like cell walls.

311. The answer is e. *(Howard, p 848.)* A distinct group of chlamydiae, first designated "TWAR," has been given the name *C. pneumoniae*. The strain was first isolated in Taiwan and usually causes mild acute respiratory disease. *C. psittaci* causes a respiratory syndrome and is associated with avian contact. *C. pneumoniae* has no avian vector. Recent evidence suggests that *C. pneumoniae* may be involved in cardiac disease, possibly as part of an autoimmune phenomenon.

312–315. The answers are 312-c, 313-e, 314-b, 315-a. *(Levinson, pp 143–144.)* Members of the mycoplasma group that are pathogenic for humans include *M. pneumoniae* and *U. urealyticum*. *M. pneumoniae* is best known as the causative agent of primary atypical pneumonia (PAP), which may be confused clinically with influenza or legionellosis. It also is associated with arthritis, pericarditis, aseptic meningitis, and the Guillain-Barré syndrome. *M. pneumoniae* can be cultivated on special media and identified by its ability to lyse erythrocytes of sheep or guinea pigs.

U. urealyticum (once called *tiny,* or *T, strain*) has been implicated in cases of nongonococcal urethritis. As the name implies, this organism is able to split urea, a fact of diagnostic significance. *U. urealyticum* is part of the normal flora of the genitourinary tract, particularly in women.

The only other species of *Mycoplasma* associated with human disease is *M. hominis*. A normal inhabitant of the genital tract of women, this organism has been demonstrated to produce an acute respiratory illness that is associated with sore throat and tonsillar exudate, but not with fever.

M. orale and *M. salivarium* are both inhabitants of the normal human oral cavity. These species are commensals and do not play a role in disease.

M. fermentans is an animal isolate.

316–320. The answers are 316-c, 317-b, 318-a, 319-e, 320-d. *(Howard, pp 856–857.)* Rickettsiae are small bacteria that are obligate, intracellular parasites. Most but not all rickettsiae are transmitted to humans by arthropods. *Coxiella* is transmitted through the respiratory tract rather than through the skin, and *B. henselae,* from animal scratches. *Coxiella* may cause chronic endocarditis that is not very responsive to either antimicrobial therapy or valve replacement. *B. henselae* is a fastidious Gram-negative rod that causes bacillary angiomatosis, a disease that forms dermal or subcutaneous nodules. The role of *B. henselae* in cat-scratch disease has recently been recognized. Molecular taxonomic studies have indicated that the causative organism is more closely related to *Bartonella* than *Rochalimaea,* hence the name change.

Ehrlichia is an obligate, intracellular parasite that resembles rickettsia. *E. chaffeensis* has been linked to human ehrlichiosis, although this infection is primarily seen in animals. The majority of patients with this disease report exposure to ticks. It is thought that *I. scapularis* carries *Ehrlichia,* although the Lone Star tick, *A. americanum,* may also transmit the disease.

Chlamydiae are Gram-negative bacteria that are obligate, intracellular parasites. They are divided into three species: *C. trachomatis, C. pneumoniae,* and *C. psittaci.* Chlamydiae have a unique developmental cycle. The infectious particle is the elementary body. Once inside the cell, the elementary body undergoes reorganization to form a reticulate body. After several replications, the reticulate bodies differentiate into elementary bodies, are released from the host cell, and become available to infect other cells. Three of the 15 serovars of *C. trachomatis* (L1, L2, L3) are known to cause lymphogranuloma venereum (LGV), a sexually transmitted disease. *C. trachomatis* is a leading cause of sexually transmitted disease in the United States. It is insidious because so many early infections are asymptomatic, particularly in women.

Rocky Mountain spotted fever is a spotted fever caused by *R. rickettsii* and is characterized by acute onset of fever, severe headache, and myalgias. The rash occurs 2 to 6 days later first in the hands and feet and then moves to the trunk. Diagnosis must be made on clinical presentations, and therapy instituted immediately. Laboratory diagnosis is made on a rising antibody titer (delayed). Untreated disease can be fatal.

Mycology

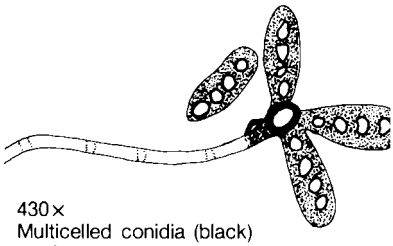
Questions

DIRECTIONS: Each question below contains five suggested responses. Select the **one best** response to each question.

321. Infected tissues demonstrating budding fungal cells are seen in

a. Coccidioidomycosis, chromomycosis, aspergillosis
b. Tinea versicolor, tinea nigra, candidiasis
c. Blastomycosis, paracoccidioides, dermatophytosis
d. Candidiasis, cryptococcosis, and sporotrichosis
e. Aspergillosis, mucormycosis, and mycetoma

322. A slide culture of a dematiaceous mold revealed the image below. The most likely identity of this mold is



430×
Multicelled conidia (black)
produced sympodially

a. *Drechslera*
b. *Cladosporium*
c. *Alternaria*
d. *Penicillium*
e. *Acremonium*

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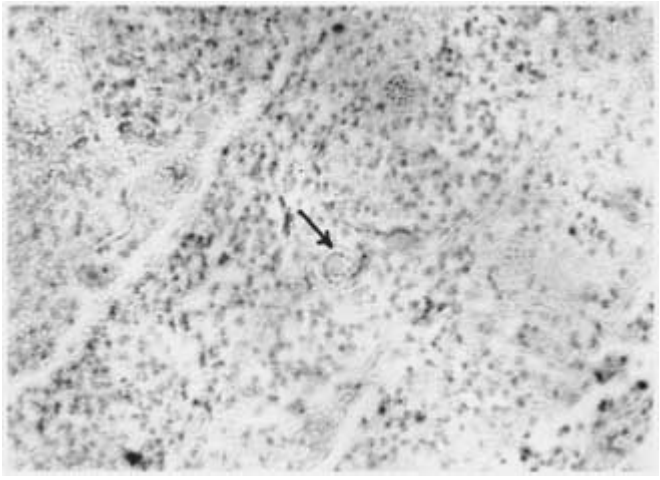
323. The object designated by the arrow in the photomicrograph below is



a. An encapsulated yeast
b. A thick-walled spore
c. A spherule
d. A hyphal strand
e. A macroconidium

324. A 6-year-old girl presents to the clinic with scaly patches on the scalp. Primary smears and culture of the skin and hair were negative. A few weeks later, she returned and was found to have inflammatory lesions. The hair fluoresced under Wood's light and primary smears of skin and hair contained septate hyphae. On speaking with the parents, it was discovered that there were several pets in the household. Which of the following is the most likely agent?

a. *Microsporum audouinii*
b. *Microsporum canis*
c. *Trichophyton tonsurans*
d. *Trichophyton rubrum*
e. *Epidermophyton floccosum*

325. A patient with AIDS has a persistent cough and has shown progressive behavioral changes in the past few weeks after eating an undercooked hamburger. A cerebrospinal fluid (CSF) sample is collected and an encapsulated, yeast-like organism is observed. Based only on these observations, what is the most likely organism?

a. *Toxoplasma*
b. *Cryptosporidium*
c. *Candida*
d. *Cryptococcus*
e. *Pneumocystis*

326. A clinical diagnosis of meningitis is confirmed with a latex agglutination test on CSF for the capsular polysaccharide of the organism. The most likely causative agent is

a. *Candida albicans*
b. *Cryptococcus*
c. *Paracoccidioides brasiliensis*
d. *Histoplasma capsulatum*
e. *Aspergillus fumigatus*

327. A section of tissue from the foot of a person assumed to have eumycotic mycetoma shows a white, lobulated granule composed of fungal hyphae. In the United States, the most common etiologic agent of this condition is a species of

a. *Acremonium*
b. *Nocardia*
c. *Actinomyces*
d. *Pseudallescheria* (*Petriellidium*)
e. *Madurella*

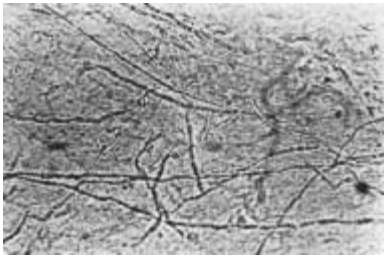
328. The formation of granulomas is seen in major systemic fungal infections. Which of the following groups of fungi is most likely to cause granulomas?

a. *Aspergillus, Coccidioides, Cryptococcus*
b. *Mucor, Candida, Malassezia*
c. *Cladosporium, Aspergillus, Microsporum*
d. *Coccidioides, Blastomyces, Histoplasma*
e. *Epidermophyton, Blastomyces, Trichophyton*

329. Infection with *Sporothrix schenckii* (formerly *Sporotrichum schenckii*) is an occupational hazard for gardeners. The portal of entry for this organism is the

a. Lymphatic system
b. Respiratory tract
c. Skin
d. Mouth
e. Mucous membranes

330. There are three genera of dermatophytes: *Epidermophyton, Microsporum,* and *Trichophyton.* Infections caused by these organisms, as shown in the figure below (dermatophytoses), are



(Courtesy of MG Rinaldi, San Antonio, TX.)

a. Marked by alveolar irritation
b. Characterized by aflatoxin-induced hallucinations
c. Confined to keratinized tissues
d. Rarely associated with chronic lesions
e. Easily treatable with penicillin

331. *C. albicans* is recognized in microscopic examination of infected tissues by the presence of

a. Spherules containing endospores
b. Metachromatic granules
c. Yeasts and pseudohyphae
d. Asci containing 2–8 ascospores
e. Abundance of septate rhizoids

332. The mechanism of mucosal invasion by *C. albicans* is at least partially understood. Which one of the following modifications in the structure or function of this yeast would be most likely to affect its invasive ability?

a. Loss of ability to produce ethanol from glucose
b. Loss of ability to produce germ tubes or hyphae
c. Reduced ability to grow at 37°C
d. Loss of ability to produce a polysaccharide capsule
e. Replacement of mannans in the cell wall with glucan

333. You have been designated as coordinator of construction of a bone marrow transplant unit (BMTU). There will be extensive removal of walls and floors in order to install the laminar flow rooms required for a BMTU. From the standpoint of frequency and lethality, which one of the following fungi should be your biggest concern?

a. *Aspergillus*
b. *Candida*
c. *Wangiella*
d. *Cryptococcus*
e. *Blastomyces*

334. *H. capsulatum,* a dimorphic fungus, is found in soil heavily contaminated with bird droppings. Which of the following statements best describes the presence of the organism in tissue biopsies?

a. Yeasts with broad-based bud
b. Single-cell yeasts with pseudohyphae
c. Arthrospores
d. Oval budding yeasts inside macrophages
e. Spherules containing endospores

335. Which of the following best describes an infection with *Coccidioides immitis*?

a. A negative complement-fixing (CF) antibody test
b. Inhaled arthrospores form thick-walled spherules filled with endospores
c. "Fungus ball" formation
d. Thrush
e. Clavate macroconidia

336. Inhalation of fungal spores can cause primary lung infections. Of the following organisms, which one is most likely to be associated with this mode of transmission?

a. *C. immitis*
b. *S. schenckii*
c. *C. albicans*
d. *T. tonsurans*
e. *Candida tropicalis*

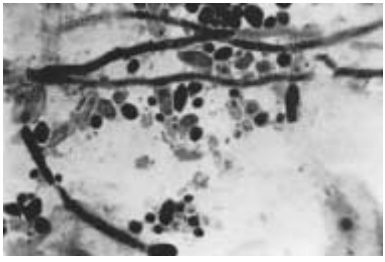
337. An immunocompromised patient is suspected of having an infection with *A. fumigatus*. Which of the clinical conditions is most likely to occur?

a. Wound infection
b. Urinary tract infection
c. Invasive aspergillosis causing thrombosis and infarction
d. Thrush
e. Superficial rash

338. Patients who have disseminated coccidioidomycosis may usually demonstrate which one of the following?

a. A negative coccidioidin skin test and a rising complement-fixing (CF) titer
b. A negative coccidioidin skin test and a stable CF titer
c. A positive skin test and a mildly elevated CF titer
d. Absence of CF antibodies
e. Lack of immunity to reinfection

339. *C. albicans* (shown below) is best described by which of the following statements?



(Courtesy of MG Rinaldi, San Antonio, TX.)

a. Widespread in environment; conidia may be inhaled; microscopic appearance in specimen reveals dichotomous branching and septate hyphae
b. Round, black sporangia filled with endospores; sporangia unbranched, rising from a runner called a *stolon*
c. Single-tipped sporangiophores; no rhizoids or stolons; nonseptate hyphae, which show branching
d. Yeast forms with budding blastoconidia often showing pseudohyphae; positive germ tube test; chlamydospores present

340. *Aspergillus* is best described by which of the following statements?

a. Widespread in environment; conidia may be inhaled; microscopic appearance in specimen reveals dichotomous branching and septate hyphae
b. Round, black sporangia filled with endospores; sporangia unbranched, rising from a runner called a *stolon*
c. Single-tipped sporangiophores; no rhizoids or stolons; nonseptate hyphae, which show branching
d. Yeast forms with budding blastoconidia often showing pseudohyphae; positive germ tube test; chlamydospores present

341. *Mucor* is best described by which of the following statements?

a. Widespread in environment; conidia may be inhaled; microscopic appearance in specimen reveals dichotomous branching and septate hyphae
b. Round, black sporangia filled with endospores; sporangia unbranched, rising from a runner called a *stolon*
c. Single-tipped sporangiophores; no rhizoids or stolons; nonseptate hyphae, which show branching
d. Yeast forms with budding blastoconidia often showing pseudohyphae; positive germ tube test; chlamydospores present

342. *Rhizopus* is best described by which of the following statements?

a. Widespread in environment; conidia may be inhaled; microscopic appearance in specimen reveals dichotomous branching and septate hyphae
b. Round, black sporangia filled with endospores; sporangia unbranched, rising from a runner called a *stolon*
c. Single-tipped sporangiophores; no rhizoids or stolons; nonseptate hyphae, which show branching
d. Yeast forms with budding blastoconidia often showing pseudohyphae; positive germ tube test; chlamydospores present

Questions 343–347

The naming of fungi is very confusing to the nonmycologist. For this reason, the clinician who may treat fungal infections should have a working knowledge of fungal taxonomy. Most of the fungi known to cause infection in humans have been recognized for many years by their asexual stage (anamorph). The sexual stage (teleomorph) of many of these familiar fungi has now been discovered.

343. The appropriate teleomorph for *Trichophyton mentagrophytes* is

a. *Ajellomyces capsulata*
b. *Ajellomyces dermatitidis*
c. *Arthroderma van breuseghemii*
d. *Filobasidiella neoformans*
e. *Nannizzia incurvata*

344. The appropriate teleomorph for *Microsporum gypseum* is

a. *Ajellomyces capsulata*
b. *Ajellomyces dermatitidis*
c. *Arthroderma van breuseghemii*
d. *Filobasidiella neoformans*
e. *Nannizzia incurvata*

345. The appropriate teleomorph for *Cryptococcus neoformans* is

a. *Ajellomyces capsulata*
b. *Ajellomyces dermatitidis*
c. *Arthroderma van breuseghemii*
d. *Filobasidiella neoformans*
e. *Nannizzia incurvata*

346. The appropriate teleomorph for *Blastomyces dermatitidis* is

a. *Ajellomyces capsulata*
b. *Ajellomyces dermatitidis*
c. *Arthroderma van breuseghemii*
d. *Filobasidiella neoformans*
e. *Nannizzia incurvata*

347. The appropriate teleomorph for *Histoplasma capsulatum* is

a. *Ajellomyces capsulata*
b. *Ajellomyces dermatitidis*
c. *Arthroderma van breuseghemii*
d. *Filobasidiella neoformans*
e. *Nannizzia incurvata*

348. Barrel-shaped arthroconidia are characteristic of which one of the following fungi?

a. *E. floccosum*
b. *C. immitis*
c. *Phialophora verrucosa*
d. *M. canis*
e. *Blastomyces dermatitidis*

349. Sporulation from flask-shaped, pigmented projections is commonly observed in which one of the following fungi?

a. *E. floccosum*
b. *C. immitis*
c. *P. verrucosa*
d. *M. canis*
e. *B. dermatitidis*

350. Clavate macroconidia are characteristic of which one of the following fungi?

a. *E. floccosum*
b. *C. immitis*
c. *P. verrucosa*
d. *M. canis*
e. *B. dermatitidis*

351. Broad-based budding cells are characteristic of which one of the following fungi?

a. *E. floccosum*
b. *C. immitis*
c. *P. verrucosa*
d. *M. canis*
e. *B. dermatitidis*

352. Rough-walled macroconidia of 8 to 15 cells are commonly observed in which one of the following fungi?

a. *E. floccosum*
b. *C. immitis*
c. *P. verrucosa*
d. *M. canis*
e. *B. dermatitidis*

Questions 353–357

Fungal skin diseases may not be named according to the etiologic agent but rather are called *tinea* or a *dermatophytosis*.

353. Tinea corporis is caused by which of the following?

a. *E. floccosum*
b. *Malassezia furfur*
c. *M. canis*
d. *Exophiala werneckii*
e. *Trichosporon beigelii*

354. Tinea cruris is caused by which of the following?

a. *E. floccosum*
b. *M. furfur*
c. *M. canis*
d. *E. werneckii*
e. *T. beigelii*

355. Tinea pedis is caused by which of the following?

a. *E. floccosum*
b. *M. furfur*
c. *M. canis*
d. *E. werneckii*
e. *T. beigelii*

356. Tinea capitis is caused by which of the following?

a. *E. floccosum*
b. *M. furfur*
c. *M. canis*
d. *E. werneckii*
e. *T. beigelii*

357. Tinea versicolor is caused by which of the following?

a. *E. floccosum*
b. *M. furfur*
c. *M. canis*
d. *E. werneckii*
e. *T. beigelii*

Questions 358–362

Harmless molds commonly seen growing on bread, as well as on a wide variety of other products or foodstuffs, grow equally well in the human host when the host's defenses are compromised.

358. Which one of the following fungi causes subcutaneous zygomycosis? It is most often seen in Africa and Asia; the infections are most often seen on the trunk or limbs and begin as painless, small nodules; and the hyphae are 6 to 25 mm in length with irregular branching:

a. *A. fumigatus*
b. *C. albicans*
c. *Conidiobolus coronata*
d. *Rhizopus arrhizus*
e. *Basidiobolus ranarum*

359. Which one of the following fungi causes subcutaneous zygomycosis? The infections usually involve the nasal area with swelling of nose and cheeks, and cases are seen in Africa with rare cases in the Caribbean and South America.

a. *A. fumigatus*
b. *C. albicans*
c. *C. coronata*
d. *R. arrhizus*
e. *B. ranarum*

360. Which one of the following fungi causes allergic bronchopulmonary disease resulting in marked elevation of serum IgE?

a. *A. fumigatus*
b. *C. albicans*
c. *C. coronata*
d. *R. arrhizus*
e. *B. ranarum*

361. Which one of the following fungi is often isolated from blood, urine, and sputum in invasive disease? It is difficult to determine whether isolation from one body site or body fluid is suggestive of colonization or infection.

a. *A. fumigatus*
b. *C. albicans*
c. *C. coronata*
d. *R. arrhizus*
e. *B. ranarum*

362. Which one of the following fungi causes rhinocerebral zygomycosis and is usually associated with acute diabetes?

a. *A. fumigatus*
b. *C. albicans*
c. *C. coronata*
d. *R. arrhizus*
e. *B. ranarum*

Mycology

Answers

321. The answer is d. *(Levinson, p 295.) Cryptococcus neoformans* causes cryptococcosis, especially cryptococcal meningitis. The organisms can be seen in cerebrospinal fluid (CSF) in india ink preparations as an oval budding yeast surrounded by a wide, unstained polysaccharide capsule. *Candida albicans,* the most important species of *Candida,* causes thrush and vaginitis, as well as other diseases. It may appear in tissue as a budding yeast or as elongated pseudohyphae (nonseptate). *Sporothrix schenckii* is a dimorphic fungus which appears as round or cigar-shaped budding yeasts in tissue. It causes a local pustule or ulcer that may become chronic.

322. The answer is a. *(Murray, pp 1164, 1300.) Drechslera* is a dematiaceous fungus that had previously been named *Helminthosporium.* Colonies are fluffy and gray to brownish-black in color. The hyphae are septate and the conidia are multiseptate and elongate. The conidiophores may be twisted.

323. The answer is b. *(Levinson, pp 289–293.)* Thick-walled spores are characteristic of many fungal infections, including blastomycosis, coccidioidomycosis, and histoplasmosis. Observation of these structures in sputum or in tissue should alert the microbiologist to a diagnosis of systemic fungal infection. The presence of encapsulated yeast in clinical specimens may suggest the presence of *Cryptococcus.*

324. The answer is b. *(Levinson, pp 287–288.)* Hairs infected with *Microsporum canis* and *M. audouini* both fluoresce with a yellow-green color under Wood's light, while *Trichophyton rubrum, T. tonsurans,* and *Epidermophyton floccosum* do not. But *M. audouini* is an anthropophilic agent of tinea capitis, whereas *M. canis* is zoophilic. *M. canis* is primarily seen in children and is associated with infected cats or dogs.

325. The answer is d. *(Levinson, p 295.)* Patients with paralysis of their cellular immune system, such as in AIDS, are susceptible to a wide variety of diseases, including infection with *Cryptococcus.* A brain abscess caused

by *C. neoformans* is not unusual in patients with AIDS. Initial laboratory suspicion is usually aroused by the presence of encapsulated yeast in the CSF. There also could be other microorganisms as well as noninfectious artifacts that superficially resemble yeast. While *C. neoformans* can be readily cultured, a rapid diagnosis can be made by detecting cryptococcal capsular polysaccharide in CSF or blood. Care must be taken to strictly control the test because rheumatoid factor may cross-react. Once the yeast is isolated, then specific stains as well as panels of assimilatory carbohydrates are available to definitively identify this organism as *C. neoformans.* The patient may also be infected with *Pneumocystis carinii,* but not in the central nervous system. *P. carinii* has recently been reclassified as a fungus.

326. The answer is b. *(Levinson, p 295.) C. neoformans* occurs widely in nature, particularly in soil contaminated with bird droppings. Human infection occurs when inhalation of the organism occurs. Lung infection is often asymptomatic but can result in pneumonia. Meningitis occurs through dissemination, particularly in immunosuppressed patients. India ink preparations of CSF reveal a budding yeast with a wide, unstained capsule in infected persons.

327. The answer is d. *(Levinson, pp 287–288.)* Eumycotic mycetoma is a slowly progressing disease of the subcutaneous tissues that is caused by a variety of fungi. The term *Madura foot* has been used to describe the foot lesion. Although several fungi have been isolated in the United States from persons who have mycetoma, *Pseudallescheria boydii* appears to be one of the most common. Other foot infections that may resemble Madura foot are actinomycotic (bacterial) in nature. These are caused by *Nocardia brasiliensis* and *Actinomadura.*

328. The answer is d. *(Levinson, p 284.)* Granuloma formation occurs in response to infection with many fungi. This cell-mediated immune response is seen in coccidioidomycosis, histoplasmosis, and blastomycosis, as well as in several others.

329. The answer is c. *(Howard, pp 600–604.)* Cutaneous sporotrichosis, caused by *S. schenckii,* begins at the site of inoculation, usually on an extremity or the face. The organism often is found on thorns of rose bushes. Ulceration is common and new lesions appear along paths of lym-

phatic channels. Extracutaneous sporotrichosis is seen primarily in bones and joints. There is no evidence to suggest that any portal of entry besides skin is important.

330. The answer is c. *(Levinson, p 287.)* The dermatophytes (see figure presented in the question) are a group of fungi that infect only superficial keratinized tissue (skin, hair, nails). They form hyphae and arthroconidia on the skin; in culture, they develop colonies and conidia. Tinea pedis, or athlete's foot, is the most common dermatophytosis. Several topical antifungal agents, such as undecylenic acid, salicylic acid, and ammoniated mercury, may be useful in treatment. For serious infection, systemic use of griseofulvin is effective.

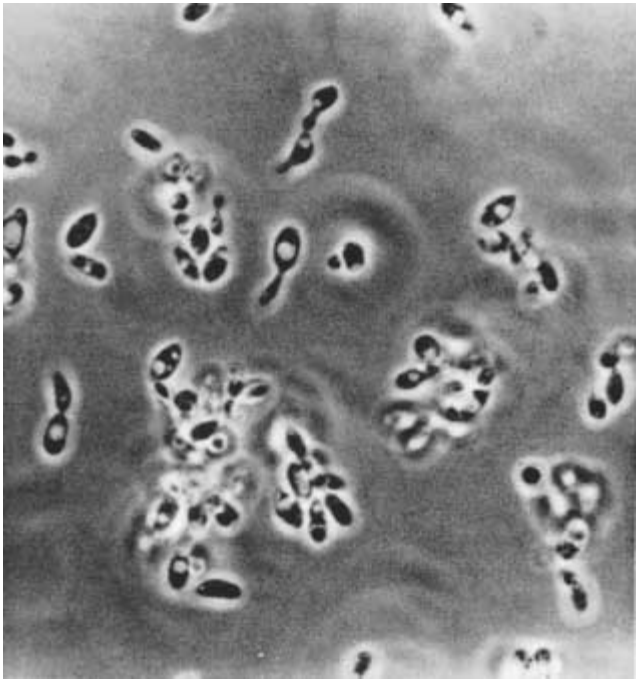
331. The answer is c. *(Levinson, pp 243–295.) C. albicans* is the most important species of *Candida* and causes thrush, vaginitis, skin and nail infections, and other infections. It is part of the normal flora of skin, mouth, GI tract, and vagina. It appears in tissues as an oval budding yeast or elongated pseudohyphae. It grows well on laboratory media and is identified by germ-tube formation. A vaccine is not available and serologic and skin tests have little value.

332. The answer is b. *(Howard, pp 616–617.) C. albicans* is part of the normal flora of the gastrointestinal tract, mouth, and genital surfaces. Notwithstanding, *C. albicans* causes severe disease particularly in those patients with compromised immunity. It is generally thought that when *C. albicans* is unable to adhere to mucosa it is nonpathogenic and that production of germ tubes or hyphae plays a major role in colonization and infection of the mucosal epithelial cells by allowing direct penetration of these cells with specific hydrolytic enzymes. While other mutations such as temperature intolerance, metabolic alterations, and structural substitutions may affect the ability of *Candida* to survive, these changes would not affect adherence.

333. The answer is a. *(Murray, pp 1217–1225.)* While all fungi such as *Candida* and *Cryptococcus* are potentially serious in a bone marrow transplant unit (BMTU), the most frequent cause of fungal infection and death is *Aspergillus*. Aspergilli are ubiquitous in the environment. There are instances of multiple infections in new units that have not been monitored

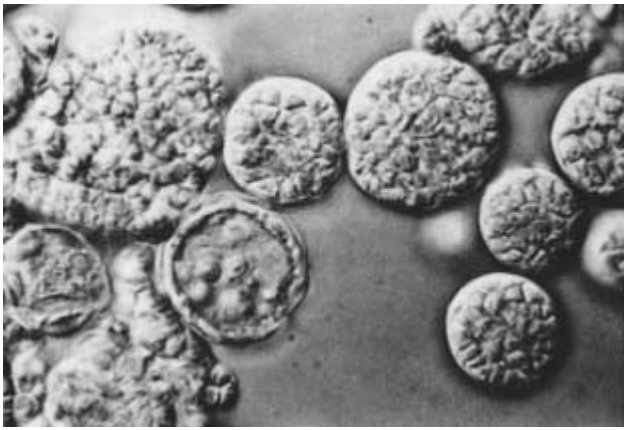
prior to opening or in units adjacent to construction projects. Strict precautions should be taken to exclude dust and debris from the BMTU area during construction, but in any event the environment should be monitored for airborne microorganisms, especially *Aspergillus,* prior to opening the unit.

334. The answer is d. *(Levinson, pp 290–291.) Histoplasma capsulatum* is a dimorphic fungus that forms two types of spores: tuberculate macroconidia and microconidia. Inhalation of the microconidia transmits infection. Inhaled spores (microconidia) are engulfed by macrophages and develop into yeast forms. Most infections remain asymptomatic; small granulomatous foci heal by calcification. However, pneumonia can occur. The heterophile antibody test is useful for early diagnosis of infectious mononucleosis. The figure below illustrates the oval budding yeasts.



Histoplasma capsulatum. Small oval yeast cells producing blastoconidia.

335. The answer is b. *(Levinson, pp 289–290.) Coccidioides immitis* is a dimorphic fungus endemic in the southwestern United States. Arthrospores found in the soil are inhaled and infect the lungs, forming large, thick-walled spherules filled with endospores. A cell-mediated immune response results in asymptomatic infection in most people. Dissemination can occur in immunocompromised persons. A delayed hypersensitivity, manifest as red nodules (erythema nodosum) on extensor surfaces such as the shins, is an indicator of good prognosis. A rising titer of complement-fixing (CF) antibodies indicates dissemination; a decrease in titer correlates with a response to therapy. The figure below illustrates the spherules filled with endospheres.



Thick-walled spherules of *Coccidioides immitis*.

336. The answer is a. *(Levinson, pp 293–295.) C. albicans* and *Candida tropicalis* are opportunistic fungi, and as part of the normal flora are not transmitted by inhalation. *C. immitis* is a dimorphic fungus and inhalation of the spores transmits the infection. *Sprothrix* is also a dimorphic fungus but its portal of entry is cutaneous. *Trychophyton* is a dermatophyte and one of the causes of athlete's foot.

337. The answer is c. *(Levinson, pp 295–296.) Aspergillus* is an opportunistic pathogen that can invade wounds, burns, abraded skin, cornea,

and outer ear. However, in immunocompromised patients, infection of the wound site is not common. *Aspergillus* does not cause urinary tract infection. In immunocompromised persons, invasive disease occurs. Blood vessel invasion can result in thrombosis and infarction. In pulmonary cavities (due to tuberculosis), "fungus ball" formation can occur, which can be seen on x-ray. Infection of the bronchi can result in allergic bronchopulmonary aspergillosis, characterized by asthmatic symptoms. Thrush is caused by *C. albicans.* Rashes are not usually seen with *Aspergillus* infection.

338. The answer is a. *(Levinson, pp 289–290.)* In patients with coccidioidomycosis, a positive skin test to coccidioidin appears 2 to 21 days after the appearance of disease symptoms and may persist for 20 years without reexposure to the fungus. A decrease in intensity of the skin response often occurs in clinically healthy people who move away from endemic areas. A negative skin test frequently is associated with disseminated disease. Complement-fixing (CF) immunoglobulin G (IgG) antibodies, which may not appear at all in mild disease, rise to a high titer in disseminated disease, a poor prognostic sign. For this reason, a persistent or rising CF titer combined with clinical symptoms indicates present or imminent dissemination. Rarely is the CF titer negative. Most persons infected with *C. immitis* are immune to reinfection.

339–342. The answers are 339-d, 340-a, 341-c, 342-b. *(Levinson, pp 293–297.)* Fungi that cause opportunistic infections are diverse, and most of them are represented in this group of questions. Infection occurs primarily in the compromised host with underlying diseases such as lymphoma, leukemia, and diabetes. Unfortunately, most of the opportunistic fungi that cause infection are commonly seen in the laboratory as contaminants.

Candidiasis is the most frequent opportunistic infection. While *C. albicans* is most commonly isolated, other species such as *C. tropicalis* and *Torulopsis glabrata* are also seen. The yeasts may be identified biochemically, but *C. albicans* is distinctive in that it produces germ tubes and chlamydospores.

Zygomycosis, a term referring to infection by members of the class Zygomycetes, is caused by *Rhizopus, Mucor,* and *Absidia* primarily. Other Zygomycetes such as *Basidiobolus* and *Cunninghamella* are rarely encountered. The lack of septate hyphae on a direct smear may be the initial hint of zygomycosis. However, not uncommonly, the occasional hypha of *Mucor* will have a septa. The genera cannot be differentiated on a direct patient specimen. The organism must be isolated and slide cultures performed to observe the characteristic morphology of these filamentous fungi.

Rhizopus species have sporangia that arise from a stolon, while *Mucor* species do not. *Mucor* species have collarettes; *Rhizopus* species do not.

Aspergillosis, caused by a number of species of *Aspergillus,* is characterized in direct smear by septate hyphae, dichotomously branched. *A. flavus* and *A. fumigatus* are often seen as saprophytes in the laboratory but also account for the major species isolated from patients with aspergillosis. Differentiation of species, as with the Zygomycetes, is dependent upon isolation of the fungus and precise morphological examination.

343–347. The answers are 343-c, 344-e, 345-d, 346-b, 347-a. *(Howard, pp 543–560.)* The classification of fungi is complicated because one pathogenic fungus (holomorph) may have two names—that of the anamorph (asexual form) and that of the teleomorph (sexual form). For example, the teleomorph of *Histoplasma capsulatum* is *Ajellomyces capsulata.* It is also interesting to note that the teleomorph (*Ajellomyces*) of two distinct genera, *Blastomyces* and *Histoplasma,* is the same. Similarly the dermatophyte *Microsporum gypseum* is the anamorph of two distinctly different sexual forms—*Nannizzia gypsea* and *N. incurvata*—and the teleomorph of *Trichophyton mentagrophytes* is *Arthroderma van breuseghemii.* The commonly known pathogenic fungus *Cryptococcus neoformans* has as its teleomorph *Filobasidiella neoformans,* a name that to date has little clinical meaning.

For those fungi in which no sexual stage has been found, the term *fungi imperfecti* serves as a convenient repository of asexual forms. In clinical practice, to avoid confusion, the name of the asexual stage is routinely reported.

348–352. The answers are 348-b, 349-c, 350-a, 351-e, 352-d. *(Levinson, pp 287, 289–290, 288, 292.)* Microscopic examination of fungal isolates is essential to the identification of the organism. Macroscopically, the colonies of *Epidermophyton* have a yellowish appearance. This fungus invades skin and nails but never hair. On microscopic examination, clavate or paddle-shaped macroconidia are evident with rounded ends and smooth walls. Microconidia are absent.

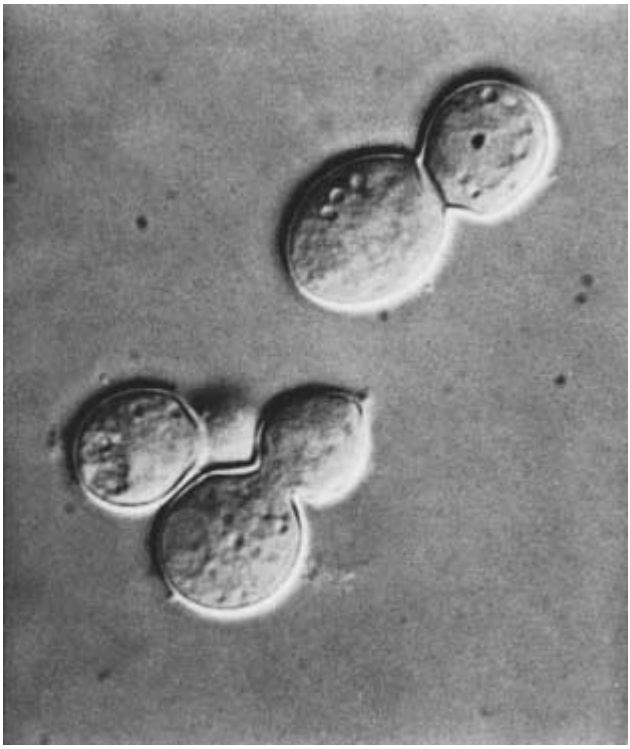
C. immitis is a dimorphic fungus endemic in some regions of the southwestern United States and in Latin America. In tissue, the organism exists as a spherule filled with endospores. When grown on solid media, the organism produces barrel-shaped arthroconidia, which stain with lactophenol cotton blue.

Phialophora verrucosa is one of the causes of chromoblastomycosis, a chronic localized infection of the skin and subcutaneous tissue. Microscop-

ically, short or somewhat elongated, flask-shaped, pigmented phialides are seen. The collarettes are vase-shaped and darkly pigmented.

M. canis is a dermatophyte that infects skin and hair but rarely nails. When hair is infected with this organism, it will fluoresce. Microscopic examination of this organism demonstrates rough-walled macroconidia of 8 to 15 cells.

Blastomyces dermatitidis causes a chronic granulomatous disease. The yeast cells are globose or ovoid in shape. The single blastoconidium is attached by a broad base to the parent cell. The following figure illustrates the broad-based budding cells.



Blastomyces dermatitidis in its yeast form. Note broad base of attachment of blastoconidium to parent cell.

353–357. The answers are 353-c, 354-a, 355-a, 356-c, 357-b. *(Levinson, p 287.)* Dermatomycoses are cutaneous mycoses caused by three genera of fungi: *Microsporum, Trichophyton,* and *Epidermophyton.* These infections are called *tinea* or *ringworm,* a misnomer that has persisted from the days when they were thought to be caused by worms or lice.

Tinea capitis (ringworm of the scalp) is due to an infection with *M. canis* or *T. tonsurans.* It usually occurs during childhood and heals spontaneously at puberty. Circular areas on the scalp with broken or no hair are characteristic of this disorder.

Tinea corporis (ringworm of the body) is caused by *M. canis* and *T. mentagrophytes.* This disorder affects smooth skin and produces circular pruritic areas of redness and scaling. Both tinea cruris (ringworm of the groin, "jock itch") and tinea pedis (ringworm of the feet, athlete's foot) are caused by *T. rubrum, T. mentagrophytes,* or *E. floccosum.* These common conditions are pruritic and can cause scaling.

Tinea versicolor (pityriasis versicolor) is not a dermatomycotic condition but, rather, a superficial mycosis now thought to be caused by *Malassezia furfur.* The disorder is characterized by chronic but asymptomatic scaling on the trunk, arms, or other parts of the body.

358–362. The answers are 358-e, 359-c, 360-a, 361-b, 362-d. *(Howard, pp 627–629.)* Candidiasis, cryptococcosis, zygomycosis, and aspergillosis are among the most common opportunistic fungal infections. These fungi are commonly observed in the environment and are innocuous to people with intact host defenses. However, when host defenses are compromised by immunosuppression (AIDS), cytotoxic drugs, diabetes, or devices that breach the normal host defenses, these usually harmless fungi become potent pathogenic microorganisms.

Lungs are the most common site for infection by *Aspergillus.* These infections range from allergic bronchopulmonary disease (with increased serum IgE), to fungus balls known as *aspergillomas,* to life-threatening invasive infections of the lung parenchyma. Typically, the fungus will spread to other organs. Patients with lymphoma, for instance, are highly susceptible to invasive aspergillosis. Death rates of 25% are not uncommon.

C. albicans is a member of the normal human microflora. This yeast causes such relatively mild infections as "jock itch" and diaper rash. Suppression of cellular immunity often results in more serious yeast infections. Oral candidiasis is one of the earliest and most frequent of the opportunis-

tic infections in patients with AIDS. Diagnosis of invasive candidiasis is difficult, especially when patients are symptomatic and *Candida* is not recovered from blood specimens. Candidal antibody tests, antigen detection, and metabolite detection have not been successful in differentiating between invasive disease and colonization. The figure presented in question 339 illustrates *C. albicans* from a skin smear.

Zygomycosis (sometimes called mucormycosis) is caused by a variety of fungi called Zygomycetes. These fungi include *Conidiobolus, Rhizopus,* and *Basidiobolus,* which can be differentiated mycologically, but all are characterized by large (6 to 25 mm), irregularly branched, usually nonseptate hyphae. The differentiation of these fungi clinically is a function of the location of the lesion: limbs and trunk, nose, or brain. *Basidiobolus* lesions are most commonly seen on the arms and legs. *Conidiobolus* is usually found in the nasal mucosa and nasal sinuses. *Rhizopus* infection may start in the nasal tissue but spreads rapidly to the eyes and brain.

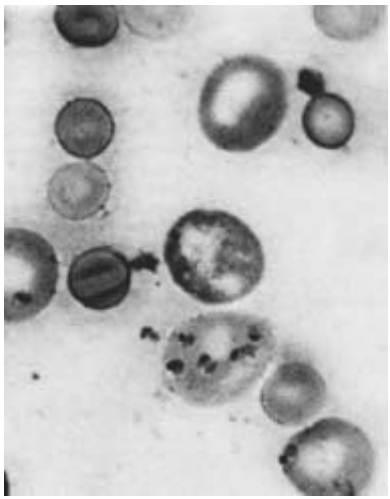
Parasitology

Questions

DIRECTIONS: Each question below contains five suggested responses. Select the **one best** response to each question.

363. Babesiosis, as observed in the figure below, is a tick-borne disease resulting in a febrile illness. Infection with *Babesia* is most commonly observed in

a. Transfusion recipients
b. Patients without a spleen
c. AIDS patients
d. Foresters
e. Transplant recipients



(Photomicrograph by Zane Price. Reproduced, with permission, from Markell EK, Voge M, and John DT: Medical Parasitology, *6/e, Philadelphia, W.B. Saunders Co., 1986.)*

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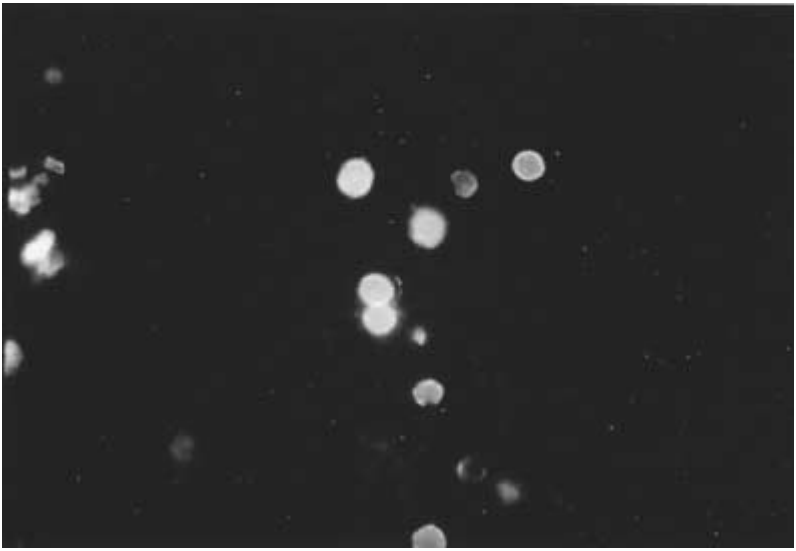
364. An AIDS patient presents to his primary care physician with a 2-week history of watery, nonbloody diarrhea. This stool revealed an organism which can be seen in the figure below. The most likely diagnosis is

a. *Cyclospora*
b. *Cryptosporidium*
c. *Enterocytozoon*
d. Yeast
e. Acid-fast bacilli

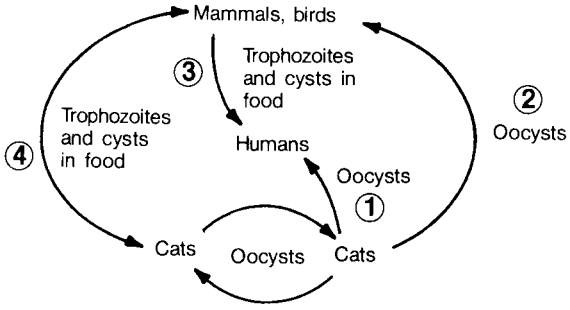


(*Reproduced, with permission, from Garcia LS:* Laboratory Methods for Diagnosis of Parasitic Infection. *In Baron EJ and Finegold SM:* Diagnostic Microbiology, *8/e, St. Louis, Mosby-Year Book: 1990.*)

365. A person who had recently consumed half a box of raspberries came down with severe watery diarrhea. Surprisingly, the patient felt tired for a few days and had a low-grade fever. The most likely cause of infection is

a. *Cryptosporidium*
b. *Escherichia coli* 0157:H7
c. *Isospora*
d. *Vibrio*
e. *Cyclospora*

366. In order to exert control over the primary cause of toxoplasmosis of pregnancy, which one of the following steps of the life cycle of *Toxoplasma* would be most practical to interrupt?

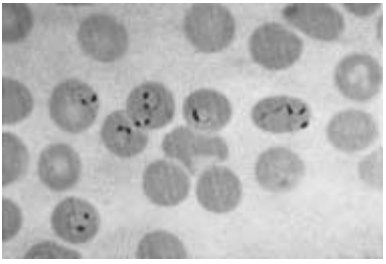


a. Step 1
b. Step 2
c. Step 3
d. Step 4
e. Steps 3 and 4

367. A 30-year-old female stored her contact lenses in tap water. She noticed deterioration of vision and visited an ophthalmologist who diagnosed her with severe retinitis. Culture of the water as well as vitreous fluid would most likely reveal

a. *Naegleria*
b. *Pneumocystis*
c. *Acanthamoeba*
d. *Babesia*
e. *Entamoeba coli*

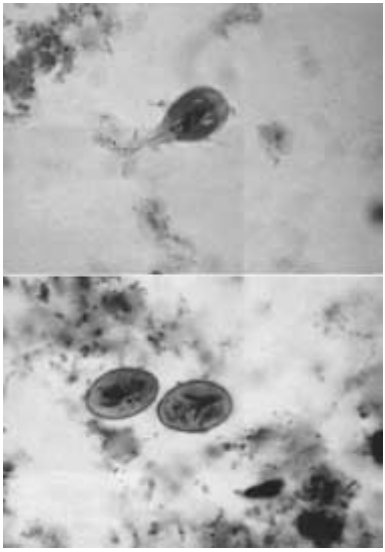
368. The diagnostic characteristics of *Plasmodium falciparum* (see figure) are best described by which one of the following statements?



(*Reproduced, with permission, from Garcia LS:* Laboratory Methods for Diagnosis of Parasitic Infection. *In Baron EJ and Finegold SM:* Diagnostic Microbiology, *8/e, St. Louis, Mosby-Year Book: 1990.*)

a. A period of 72 h is required for the development of the mature schizont, which resembles a rosette with only 8 to 10 oval merozoites
b. An important diagnostic feature is the irregular appearance of the edges of the infected red blood cell
c. The signet-ring–shaped trophozoite is irregular in shape with ameboid extensions of the cytoplasm
d. Except in infections with very high parasitemia, only ring forms of early trophozoites and the gametocytes are seen in the peripheral blood
e. Schüffner stippling is routinely seen in red blood cells that harbor parasites

369. The life cycle of this parasite consists of two stages: the cyst and the trophozoite, as shown in the figure below. The most likely identification of this organism is



(*Reproduced, with permission, from Garcia LS:* Laboratory Methods for Diagnosis of Parasitic Infections. *In Baron EJ and Finegold SM:* Diagnostic Microbiology, 8/e, *St. Louis, Mosby-Year Book: 1990.*)

a. *Entamoeba*
b. *Clonorchis*
c. *Giardia*
d. *Trichomonas*
e. *Pneumocystis*

370. A recently recognized organism secretes potent toxins, has been responsible for significant fish kills, and has also caused disease in humans. This organism has been identified as

a. *Listeria monocytogenes*
b. *Giardia lamblia*
c. *Vibrio parahaemolyticus*
d. *Pfiesteria piscicida*
e. *Aeromonas salmonicida*

371. Human infection with the beef tapeworm, *Taenia saginata,* usually is less serious than infection with the pork tapeworm, *T. solium,* because

a. Acute intestinal stoppage is less common in beef tapeworm infection
b. Larval invasion does not occur in beef tapeworm infection
c. Toxic by-products are not given off by the adult beef tapeworm
d. The adult beef tapeworms are smaller
e. Beef tapeworm eggs cause less irritation of the mucosa of the digestive tract

372. A man coughed up a long (4 to 6 cm) white worm and his chief complaint was abdominal tenderness. He reports that he goes to sushi bars at least once a week. The following parasites have been observed in people who eat raw fish: *Anisakis, Pseudoterranova, Eustrongylides,* and *Angiostrongylus.* Which of the following would best differentiate the specific parasitic agent?

a. Identification of specific species of fish involved
b. Study of distinctive morphology of the parasite
c. Specific antibody tests
d. Antigen detection in tissues
e. Characteristic signs and symptoms

373. A survey of 100 healthy adults reveals that 80% have IgG antibodies to *Toxoplasma*. Which one of the following statements would help to explain this finding?

a. The potential for *Toxoplasma* infection is widespread and the disease is mild and self-limiting
b. Toxoplasmosis is caused by eating meat; therefore, all meat eaters have had toxoplasmosis
c. A variety of parasitic infections induce the formation of *Toxoplasma* antibody
d. The test for *Toxoplasma* antibodies is highly nonspecific
e. The IgM test is more reliable than the IgG test for determination of past infections; retesting for IgM would show that most people do not have *Toxoplasma* antibody

374. In the United States, certain enteric protozoan and helminthic infections were previously considered to be exotic illnesses related to foreign travel or to contaminated food or water. However, sexual transmission of these diseases has produced a "hyperendemic" infection rate among male homosexuals. The most common infection seen in this group is

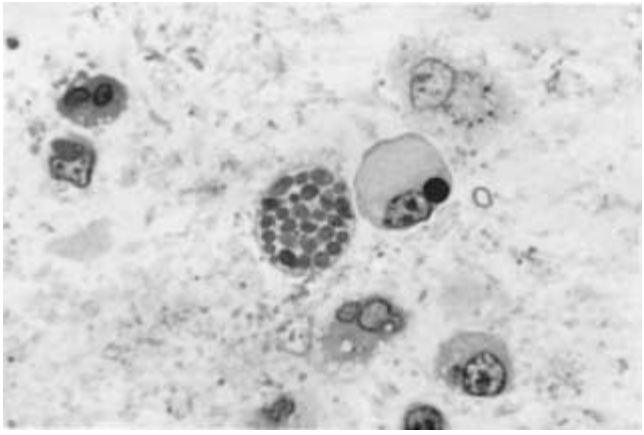
a. Giardiasis
b. Ascariasis
c. Amebiasis
d. Enterobiasis
e. Trichuriasis

375. Analysis of a patient's stool reveals small structures resembling rice grains; microscopic examination shows these to be proglottids. The most likely organism in this patient's stool is

a. *Enterobius vermicularis*
b. *Ascaris lumbricoides*
c. *Necator americanus*
d. *T. saginata*
e. *Trichuris trichiura*

376. An AIDS patient complains of headaches and disorientation. A clinical diagnosis of *Toxoplasma encephalitis* is made and *Toxoplasma* cysts were observed in a brain section (see figure below). Which one of the following antibody results would be most likely in this patient?

a. IgM nonreactive, IgG nonreactive
b. IgM nonreactive, IgG reactive (low titer)
c. IgM reactive (low titer), IgG reactive (high titer)
d. IgM reactive (high titer), IgG reactive (high titer)
e. IgM reactive (high titer), IgG nonreactive



377. *Trypanosoma cruzi* initially penetrates through the mucous membranes on the skin and then multiplies in a lesion known as a *chagoma.* In the chronic stage of the disease, the main lesions are often observed in the

a. Spleen and pancreas
b. Heart and digestive tract
c. Liver and spleen
d. Digestive tract and respiratory tract
e. Heart and liver

378. A woman, recently returned from Africa, complains of having paroxysmal attacks of chills, fever, and sweating; these attacks last a day or two at a time and recur every 36 to 48 h. Examination of a stained blood specimen reveals ringlike and crescent-like forms within red blood cells. The infecting organism most likely is

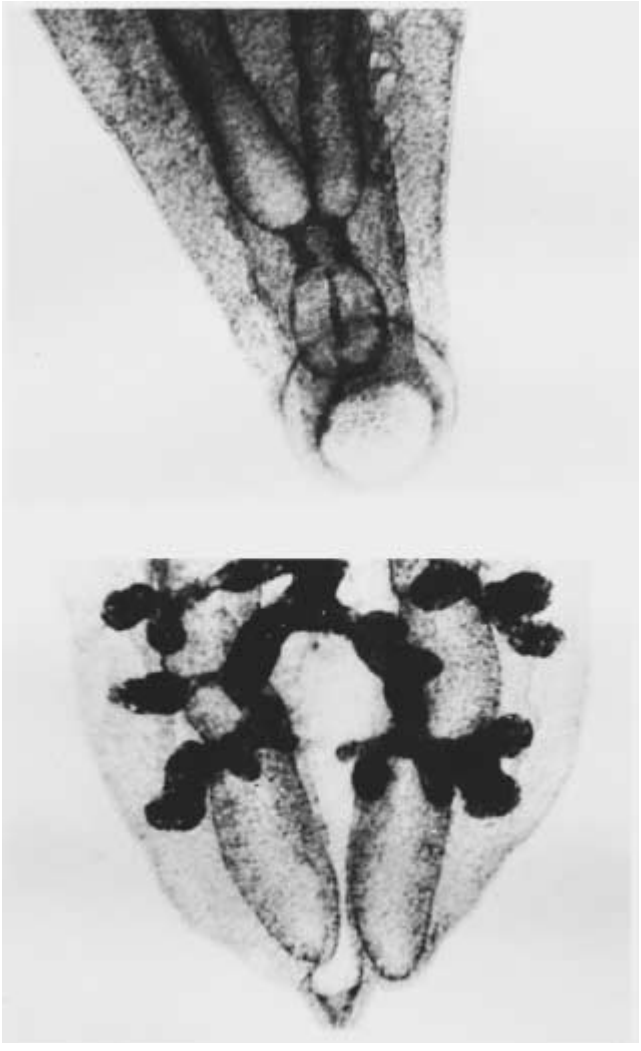
a. *Plasmodium falciparum*
b. *Plasmodium vivax*
c. *Trypanosoma gambiense*
d. *Wuchereria bancrofti*
e. *Schistosoma mansoni*

Questions 379–380

A young man, recently returned to the United States from Vietnam, has severe liver disease. Symptoms include jaundice, anemia, and weakness.

379. The etiologic agent, shown in the photomicrographs below, is

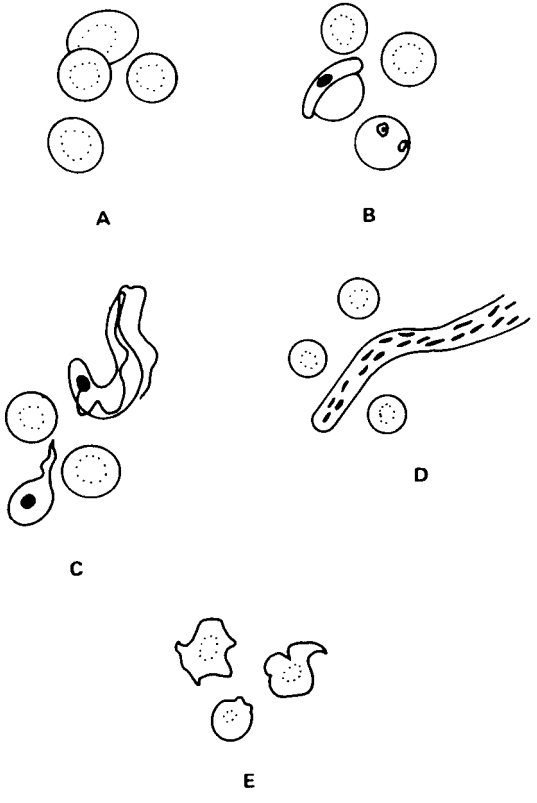
a. *P. falciparum*
b. *Clonorchis sinensis*
c. *Diphyllobothrium latum*
d. *T. solium*
e. *T. saginata*



380. An intermediate form of the organism shown in the photomicrographs on the preceding page lives in

a. Mosquitoes
b. Pigs
c. Snails
d. Cows
e. Ticks

381. A woman who recently traveled through Central Africa now complains of severe chills and fever, abdominal tenderness, and darkening urine. Her febrile periods last for 28 h and recur regularly. Which of the blood smears drawn below would most likely be associated with the symptoms described?



a. A
b. B
c. C
d. D
e. E

382. One of the most clinically significant infections in patients with AIDS is *Pneumocystis carinii* pneumonia (PCP). PCP is a treatable disease; therefore, rapid diagnosis is essential. The method of choice for detection of *P. carinii* in respiratory specimens is

a. Methenamine-silver stain
b. Toluidine blue stain
c. Direct fluorescent antibody (DFA) microscopy
d. Indirect fluorescent antibody (IFA) microscopy
e. Culture in rat lung cells

383. There are five varieties of cockroaches: the German cockroach, the brown-banded cockroach, the oriental cockroach, the American cockroach, and the smoky brown cockroach. A characteristic of cockroaches is their

a. Transmission of *Salmonella*
b. Toxic sting
c. Function as a vector for *Borrelia burgdorferi*
d. Function as a secondary host for rickettsiae
e. Easy eradication

384. The photomicrograph below shows fine fibrils (labeled F) in an ameba. These structures are

a. Termed *amebic microtubules*
b. Analogous to actin in the cells of higher forms of life
c. Primarily of glycoprotein composition
d. Not involved in cell motility
e. Inactive at 37°C (98.6°F)

385. A "parasite" that may be a fungus is the initial clinical manifestation in up to 60% of patients with AIDS. This organism is

a. Microsporidium
b. *Cryptosporidium*
c. *Pneumocystis*
d. *Blastocystis*
e. *Blastomyces*

386. A medical technologist visited Scandinavia and consumed raw fish daily for 2 weeks. Six months after her return home, she had a routine physical and was found to be anemic. Her vitamin B_{12} levels were below normal. The most likely cause of her vitamin B_{12} deficiency anemia is

a. Excessive consumption of ice-cold vodka
b. Infection with parvovirus B 19
c. Infection with the fish tapeworm *D. latum*
d. Infection with *Yersinia*
e. Cysticercosis

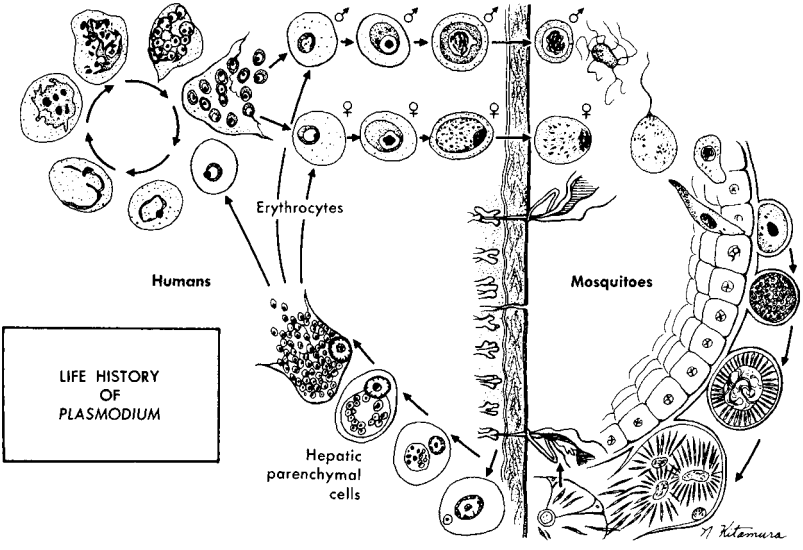
387. A renal transplant patient was admitted for graft rejection and pneumonia. A routine evaluation of his stool showed rhabditiform larvae. Subsequent follow-up revealed similar worms in his sputum. He had no eosinophils in his peripheral circulation. The most likely organism is

a. *Necator*
b. *Hymenolepsis*
c. *Ascaris*
d. *Loa loa*
e. *Strongyloides*

388. Which of the following best describes lice?

a. They have wings
b. They cause tissue edema
c. They transmit epidemic typhus, relapsing fever, and trench fever
d. *Pediculus humanus* is the only species of louse
e. They secrete a potent neurotoxin

389. Malaria is a significant worldwide public health problem. The life cycle of *Plasmodium* can be seen in the figure below. Which one of the following control methods for malaria is currently effective?



a. A vaccine
b. Chemoprophylaxis
c. Antibiotics
d. White clothing
e. Tick repellents

390. Scabies is caused by a small mite that burrows into the skin. The disease is best described by which one of the following statements?

a. It is caused by a species of *Sarcoptes*
b. Secondary bacterial infection is rare
c. It is synonymous with Kawasaki's syndrome
d. It is best diagnosed by biopsy of the inflammatory region around the mite bite
e. Allergic (asthma-like) reactions to mites are rare

391. Amebae that are parasitic in humans are found in the oral cavity and the intestinal tract. Which one of the following statements best describes these intestinal amebae?

a. They are usually nonpathogenic
b. They can cause peritonitis and liver abscesses
c. They are usually transmitted as trophozoites
d. They occur most abundantly in the duodenum
e. Infection with *Entamoeba histolytica* is limited to the intestinal tract

392. Schistosomiasis is a disease characterized by granulomatous reactions to the ova or to products of the parasite at the place of oviposition. Clinical manifestations include which one of the following?

a. Bladder wall hyperplasia
b. Pulmonary embolism
c. Splenomegaly
d. Cardiac abnormalities
e. Arthropathies

393. *B. burgdorferi,* the causative agent of Lyme disease, has been isolated from a variety of ticks such as *Ixodes scapularis, Amblyomma, Dermacentor,* and *Ixodes pacificus*. Which one of the following statements is true of Lyme disease?

a. *I. scapularis* and *I. dammini* are different types of ticks
b. White-tailed deer, an important reservoir for *I. scapularis,* are dying because of Lyme disease
c. Only a small percentage of people who get bitten by a tick develop Lyme disease
d. *Dermacentor* and *Amblyomma* are significant vectors of *B. burgdorferi* to humans
e. Dogs and cats are naturally immune to Lyme disease

394. Microsporidia are spore-forming, obligate, intracellular parasites. Which of the following statements best describes microsporidia?

a. There is one genus of microsporidia
b. Microsporidia have been detected only in patients with AIDS
c. Microsporidia are too small to be observed in stool specimens even with the use of special stains
d. Microsporidia are found only in a variety of vertebrate and invertebrate hosts
e. A serologic test is the only diagnostic tool for microsporidiosis

Questions 395–398

Flukes (trematodes) have a great impact on worldwide public health, causing both morbidity and mortality.

395. Which of the following organisms penetrates skin, is endemic in Africa and Latin America, and has a large lateral spine on its eggs?

a. *Paragonimus*
b. *Clonorchis*
c. *S. mansoni*
d. *Schistosoma japonicum*
e. *Schistosoma haematobium*

396. Which of the following organisms may be ingested with raw fish, affects the liver, and has an operculated egg?

a. *Paragonimus*
b. *Clonorchis*
c. *S. mansoni*
d. *S. japonicum*
e. *S. haematobium*

397. Which of the following organisms penetrates skin, is endemic in Asia, and has a small lateral spine on its eggs?

a. *Paragonimus*
b. *Clonorchis*
c. *S. mansoni*
d. *S. japonicum*
e. *S. haematobium*

398. Which of the following organisms penetrates skin, is endemic in Africa and the Middle East, has large terminal spines on its eggs, and is found in urine samples?

a. *Paragonimus*
b. *Clonorchis*
c. *S. mansoni*
d. *S. japonicum*
e. *S. haematobium*

Questions 399–402

A primary procedure for diagnosis of fecal parasites is a stained smear of feces. For some parasitic infections, however, other specimens may be more productive.

399. *G. lamblia* is best diagnosed by

a. Sigmoidoscopy and aspiration of mucosal lesions
b. Baermann technique
c. Dilution followed by egg count
d. Enzyme immunoassay (EIA)
e. Examination of a cellophane tape swab

400. *E. histolytica* infection is best diagnosed by

a. Sigmoidoscopy and aspiration of mucosal lesions
b. Baermann technique
c. Dilution followed by egg count
d. Enzyme immunoassay (EIA)
e. Examination of a cellophane tape swab

401. The best method for the detection of *Strongyloides* larvae is

a. Sigmoidoscopy and aspiration of mucosal lesions
b. Baermann technique
c. Dilution followed by egg count
d. Enzyme immunoassay (EIA)
e. Examination of a cellophane tape swab

402. *Ascaris* are best observed in human specimens by which one of the following?

a. Sigmoidoscopy and aspiration of mucosal lesions
b. Baermann technique
c. Dilution followed by egg count
d. Enzyme immunoassay (EIA)
e. Examination of a cellophane tape swab

Questions 403–407

403. A butcher, who is fond of eating raw hamburger, develops chorioretinitis; a Sabin-Feldman dye test is positive. This patient is most likely infected with

a. Trichinosis
b. Schistosomiasis
c. Toxoplasmosis
d. Visceral larva migrans
e. Giardiasis

404. A fur trapper complains of sore muscles, has swollen eyes, and reports eating bear meat on a regular basis. He is at risk for

a. Trichinosis
b. Schistosomiasis
c. Toxoplasmosis
d. Visceral larva migrans
e. Giardiasis

405. A newspaper correspondent has diarrhea for 2 weeks following a trip to St. Petersburg (Leningrad). You might expect him to have

a. Trichinosis
b. Schistosomiasis
c. Toxoplasmosis
d. Visceral larva migrans
e. Giardiasis

406. A retired Air Force colonel has had abdominal pain for 2 years; he makes yearly freshwater fishing trips to Puerto Rico and often wades with bare feet into streams. Which of the following should be in your differential diagnosis?

a. Trichinosis
b. Schistosomiasis
c. Toxoplasmosis
d. Visceral larva migrans
e. Giardiasis

407. A teenager who works in a dog kennel after school has had a skin rash, eosinophilia, and an enlarged liver and spleen for 2 years. The most likely cause of this infection is

a. Trichinosis
b. Schistosomiasis
c. Toxoplasmosis
d. Visceral larva migrans
e. Giardiasis

Questions 408–412

Certain parasites are found most commonly in particular body contents.

408. A protozoan with characteristic jerky motility is most commonly observed in

a. Vaginal secretions
b. Duodenal contents
c. Blood
d. Biopsied muscle
e. Sputum

409. A helminth that is naturally transmitted by ingestion of pork, bear, or walrus meat could be detected in

a. Vaginal secretions
b. Duodenal contents
c. Blood
d. Biopsied muscle
e. Sputum

410. A tissue-dwelling trematode that may be found in feces can also be detected in

a. Vaginal secretions
b. Duodenal contents
c. Blood
d. Biopsied muscle
e. Sputum

411. Cysts of a protozoan adhere to a piece of nylon yarn coiled in a gelatin capsule which is swallowed. These cysts are usually found in

a. Vaginal secretions
b. Duodenal contents
c. Blood
d. Biopsied muscle
e. Sputum

412. A parasite resembling malaria that infects both animals and humans and is carried by the same tick that transmits *B. burgdorferi* (the bacterium that causes Lyme disease) would most likely be observed in

a. Vaginal secretions
b. Duodenal contents
c. Blood
d. Biopsied muscle
e. Sputum

Parasitology

Answers

363. The answer is b. *(Levinson, pp 313–314.) Babesia* is a tick-borne organism transmitted by *Ixodes scapularis,* the same tick that transmits Lyme disease. *Babesia* is often mistaken for *Plasmodia* (causative organism of malaria) on a blood smear. Patients become anemic and develop hepatosplenomegaly, but patients who are asplenic are at a much greater risk. Transfusion recipients, foresters, and immunosuppressed patients may be at risk of acquiring disease but not to the same extent as these patients who have been splenectomized.

364. The answer is b. *(Levinson, pp 302–303.)* The figure presented in the question shows a *Cryptosporidium* oocyst stained with a fluorescent-labeled specific antibody. *Cryptosporidium* may also be stained with a modified acid-fast stain but are not acid-fast bacilli. They are smaller than *Cyclospora,* which are yeast size, but larger than *Enterocytozoon,* one of the microsporidia.

365. The answer is e. *(Murray, pp 1406–1412.)* Cyclosporiasis is a newly recognized food- and water-borne infectious disease associated with eating contaminated berries imported from some Central American countries. *Cyclospora* are moderately acid-fast but twice the size of *Cryptosporidium.* Patients usually have frequent diarrhea for up to 3 weeks and usually suffer only malaise and fatigue. The disease is self-limiting, but relapses can occur.

366. The answer is a. *(Levinson, pp 306–307.) Toxoplasma gondii* may be acquired by inhalation of oocysts in cat feces. It is difficult to control the habits of cats unless they are housed and not let out. Pregnant human females should avoid changing cat litter boxes. While ingestion of oocysts in raw meat may also lead to toxoplasmosis, inhalation of oocysts is the primary cause, particularly among pregnant women in the United States.

367. The answer is c. *(Levinson, p 313.) Acanthamoeba* is a free-living ameba as is *Naegleria. Naegleria* usually causes severe, often fatal, menin-

goencephalitis, while *Acanthamoeba* is uncommonly isolated from contact lens fluid and patients with retinitis who do not store their lenses under sterile conditions. Acanthamoeba can be grown on nonnutrient agar plates using *Escherichia coli* as a food source. They are identified microscopically with use of a nonspecific fluorescent stain.

368. The answer is d. *(Levinson, pp 304–306.) Plasmodium falciparum* infection is distinguished by the appearance of ring forms of early trophozoites and gametocytes, both of which can be found in the peripheral blood. The size of the RBC is usually normal. Double dots in the rings are common.

369. The answer is c. *(Levinson, p 302.) Giardia* exists in both trophozoite and cyst form. The "trophs" are fragile and not commonly seen in stools. The cysts are infectious. *Giardia* is the most common parasitic disease in the United States. It is commonly contracted from drinking cyst-contaminated water. Chlorine does not kill *Giardia* cysts but contaminated water can be made cyst-free by filtration.

370. The answer is d. *(ASM News, 1997, pp 590–592.) Pfiesteria* is a toxin-producing dinoflagellate with a complex life cycle. *Pfiesteria* can live either as a plant or a dinoflagellate. It has been responsible for massive fish kills due to algal "blooms." Such blooms are commonly called *tides.* Red tides, and the like, are also responsible for many cases of human food poisoning.

371. The answer is b. *(Ash, pp 322–327.)* Both beef tapeworm (*Taenia saginata*) and pork tapeworm (*T. solium*) can, in the adult form, cause disturbances of intestinal function. Intestinal disorder is due not only to direct irritation but also to the action of metabolic toxic wastes. In addition, *T. saginata,* because of its large size, may produce acute intestinal blockage. Unlike *T. saginata, T. solium* produces cysticercosis, which results in serious lesions in humans (in *T. saginata,* the cysticercus—encysted larvae stage—develops only in cattle).

372. The answer is b. *(Levinson, p 298.)* The consumption of raw fish products in Asian restaurants, especially the growing popularity of sushi and sashimi, has led to a variety of infections, most of which are character-

ized by symptoms consistent with intestinal blockage or meningitis. The parasites are tissue nematodes and parasites of marine mammals. Fish, squid, and other edible marine life are often secondary hosts. The most reliable way to differentiate the specific helminth is by examination of the whole worm or by histologic examination of the parasites in tissue sections.

373. The answer is a. *(Levinson, pp 306–307.)* Serologic tests, such as the Sabin-Feldman dye test and indirect immunofluorescence, have shown that a high percentage of the world's population has been infected with *Toxoplasma gondii*. In adults, clinical toxoplasmosis usually presents as a benign syndrome resembling infectious mononucleosis. However, fetal infections are often severe and associated with hydrocephalus, chorioretinitis, convulsions, and death. Acute toxoplasmosis is best diagnosed by an IgM capture assay. In most patients, specific IgM antibody disappears within 3 to 6 months.

374. The answer is a. *(Ash, pp 99, 106, 107, 118, 119.)* The infection rate with *Giardia lamblia* in male homosexuals has been reported to be from 21 to 40%. These high prevalence rates are probably related to three factors: the endemic rate, the sexual behavior that facilitates transmission (the usual barriers to spread have been interrupted), and the frequency of exposure to an infected person.

375. The answer is d. *(Ash, pp 32, 33, 231, 233, 322, 327.)* *Enterobius* (pinworm), *Ascaris* (roundworm), *Necator* (hookworm), and *Trichuris* (whipworm) are roundworms, or nematodes. *T. saginata* (tapeworm), a segmented flatworm, affects the small intestine of humans. Tapeworm segments, called proglottids, appear in the stool of infected persons.

376. The answer is b. *(Levinson, pp 306–307.)* One of the leading causes of death among AIDS patients is central nervous system toxoplasmosis. It is thought that *Toxoplasma* infection is a result of reactivation of old or preexisting toxoplasmosis. Occasionally, the infection may be acquired by needle sharing. Because the disease is a reactivation of old or preexisting toxoplasmosis, routine quantitative tests for IgM antibody are usually negative and IgG titers are low (≤1:256, IFA). More sophisticated methods, such as IgM capture or IgG avidity, may reveal an acute response.

377. The answer is b. *(Ash, pp 174–177.)* American trypanosomiasis (Chagas' disease) is produced by *Trypanosoma cruzi,* which is transmitted to humans by the bite of an infected reduviid bug. After multiplication, the tissues most likely to be affected in the chronic stage of the disease are the cardiac muscle fibers and the digestive tract. A diffuse interstitial fibrosis of the myocardium results and may lead to heart failure and death. The inflammatory lesions in the digestive tract that are seen in the esophagus and colon produce considerable dilatation. Chagas' disease has not been an important disease in the United States; most cases have been imported, although there are a few reports of endogenous disease in the southern United States.

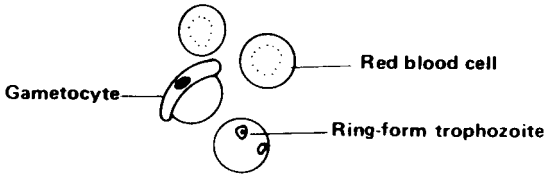
378. The answer is a. *(Ash, pp 160–163.)* The febrile paroxysms of *Plasmodium malariae* malaria occur at 72-h intervals; those of *P. falciparum* and *P. vivax* malaria occur every 48 h. The paroxysms usually last 8 to 12 h with *P. vivax* malaria but can last 16 to 36 h with *P. falciparum* disease. In *P. vivax, P. ovale,* and *P. malariae* infections, all stages of development of the organisms can be seen in the peripheral blood; in malignant tertian (*P. falciparum*) infections, only early ring stages and gametocytes are usually found.

379. The answer is b. *(Ash, pp 289–291.)* The Chinese liver fluke, *Clonorchis sinensis,* is a parasite of humans that is found in Japan, China, Korea, Taiwan, and Indochina. Humans usually are infected by eating uncooked fish. The worms invade bile ducts and produce destruction of liver parenchyma. Anemia, jaundice, weakness, weight loss, and tachycardia may follow. Treatment is likely to be ineffectual in heavy infections, but chloroquine can destroy some of the worms.

380. The answer is c. *(Ash, pp 289–291.)* The life cycle of *C. sinensis* is similar to that of other trematodes. A mollusk is characteristically the first intermediate host of trematodes. For *C. sinensis,* snails perform this role.

381. The answer is b. *(Ash, pp 160–163.)* The case history presented in the question is characteristic of infection with *P. falciparum,* the causative agent of malignant tertian malaria. The long duration of the febrile stage rules out other forms of malaria. The presence of ringlike young trophozoites and crescent-like mature gametocytes—as represented in the

illustration below—as well as the absence of schizonts is diagnostic of *P. falciparum* malaria.



382. The answer is c. *(Levinson, p 308.)* Both methenamine-silver and toluidine blue stain pneumocysts nonspecifically. These preparations are difficult to read because background material may nonspecifically stain black or blue. *Pneumocystis carinii* cannot be routinely cultured from human specimens. Both IFA and DFA tests are FDA-approved and available for detection of *P. carinii.* The advantage of DFA is that it is quicker (45 to 60 min versus 3 h) and there is less nonspecific fluorescence observed in the preparation. Recent evidence suggests that *Pneumocystis* is a fungus.

383. The answer is a. *(Murray, pp 1456–1457.)* Cockroaches are nuisances and multiply rapidly in homes, hospitals, and factories. While sprays may be effective, roaches often hide in places not reached by sprays. The biggest public health problem with roaches is that they may carry *Salmonella* and contaminate food or surfaces that they contact.

384. The answer is b. *(Ash, pp 63, 118, 119.)* The movement of amebic trophozoites is usually unidirectional and controlled in part by chemotactic factors in the immediate environment. Amebae are motile by virtue of pseudopods, which are cytoplasmic extensions that alternately project and contract. The fibrils shown in the amebic pseudopod presented in the figure in the question are involved in cellular motility and are similar to muscle actin. Amebic motility is retarded as environmental temperature falls below 37°C (98.6°F).

385. The answer is c. *(Howard, pp 680–681.)* One of the multiple criteria for classification of AIDS is the development of *P. carinii* pneumonia (PCP). *Pneumocystis* is a fungus formerly thought to be a parasite that was classified with the sporozoa. PCP may also be seen in patients with con-

genital or other acquired cellular immune dysfunction. Most patients with AIDS are given prophylactic aerosolized pentamidine or SXT-TMP for PCP. PCP is easily diagnosed in respiratory secretions by a direct fluorescent antibody test. Both the microsporidia and *Cryptosporidium* are intestinal parasites that also infect patients with AIDS, but these microorganisms cause protracted diarrhea. *Blastocystis* and *Blastomyces* are both yeasts and should not be confused with *Pneumocystis* or each other.

386. The answer is c. *(Howard, pp 680–681.)* Consumption of raw fish causes endemic diphyllobothriasis in Scandinavia and the Baltic countries. While most people do not become ill, a small percentage (2%) develop vitamin B_{12} deficiency anemia. The adult fish tapeworm has an affinity for vitamin B_{12} and may induce a serious megaloblastic anemia. Parvovirus B 19 causes acute hemolytic anemia primarily in immunosuppressed patients. *Yersinia* infection is common in Scandinavia but is not fish-borne and does not cause anemia. The larval stage of *T. solium* is called *cysticercus*. Humans usually acquire cysticercosis by ingestion of food and water contaminated by infected human feces.

387. The answer is e. *(Howard, pp 672–675.)* Strongyloidiasis may be observed in three phases: cutaneous, pulmonary, and intestinal. The pulmonary presentation of *Strongyloides* in patients with AIDS is the most common. Often, all body fluids will contain larvae. Prognosis is poor. *Necator* must be distinguished from *Strongyloides* by microscopy. Gross appearances are similar.

388. The answer is c. *(Murray, pp 747–748.) Pediculus humanus* (head or body louse) and *Phthirus pubis* (crab louse) are wingless parasites exclusively affecting humans. Lice are important not only for the itching and discomfort they cause but also for the diseases they transmit. These disorders include epidemic typhus, relapsing fever, and trench fever. There is no evidence that lice secrete toxins.

389. The answer is b. *(Levinson, pp 304–306.)* Prophylaxis for malaria should be considered whenever traveling in a malaria-endemic area. Drugs consist of mefloquine or chloroquine and Fansidar. Other control measures such as draining swamps, protective clothing and netting, and insect repellents are also effective. There is no currently available vaccine for malaria.

390. The answer is a. *(Murray, pp 1462–1463.) Sarcoptes scabiei* is a small mite that burrows into human skin. Itching is significant, and a vesicular eruption, which often becomes secondarily infected with bacteria, develops. Diagnosis is made by microscopic detection of the mites. Gamma benzene hexachloride (Kwell), a topical insecticide, is an effective treatment for scabies. A number of etiologic agents have been proposed for Kawasaki's disease (KD), among them mites, but there is no evidence that mites either cause or are vectors of KD.

391. The answer is b. *(Levinson, pp 299–302.)* Of the intestinal amebae, *Entamoeba hartmanni, E. coli, E. polecki,* and *E. nana* are considered nonpathogenic. *E. histolytica* is distinctively characterized by its pathogenic potential for humans, although infection with this protozoan is commonly asymptomatic (causing "healthy carriers"). Symptomatic amebiasis and dysentery occur when the trophozoites invade the intestinal wall and produce ulceration and diarrhea. Peritonitis can occur, with the liver the most common site of extraintestinal disease. The life cycle of the ameba is simple. There is encystment of the troph, followed by excystation in the ileocecal region. The trophs multiply and become established in the cecum, where encystation takes place and results in abundant amebae, cysts, and trophozoites. Infection is spread by the cysts, which can remain for weeks or months in appropriately moist surroundings.

392. The answer is c. *(Ash, pp 302–307.)* Although the chronic stage of proliferation within tissues is distinctive in the different forms of schistosomiasis, a granulomatous reaction to the eggs and chemical products of the schistosome occurs in all forms of the disease. *Schistosoma haematobium* commonly involves the distal bowel and the bladder, as well as the prostate gland and seminal vesicles. Bladder calcification and cancer may ensue. *S. mansoni* affects the large bowel and the liver; presinusoidal portal hypertension, splenomegaly, and esophageal varices may be complications. Pulmonary hypertension, often fatal, may be seen with *S. mansoni* and *S. japonicum* disease. Eggs may be found in an unstained specimen of rectal mucosa or in stool. Urine microscopy and liver biopsy, when warranted, often prove positive. Schistosomiasis is best prevented by the elimination of the parasite in snails before human infection occurs.

393. The answer is c. *(Levinson, pp 147–148.)* In the United States, *Borrelia burgdorferi,* the causative agent of Lyme disease, has two principal vectors:

I. scapularis in the eastern and midwestern United States and *I. pacificus* in the western United States. The ticks are tiny and can easily be missed. Fortunately, relatively few people who are bitten by ticks develop Lyme disease. Lyme disease, usually with joint involvement, is also seen in veterinary patients such as dogs, cats, and horses. White-tailed deer and small rodents are an important reservoir for these ticks. *B. burgdorferi* has been isolated from mosquitoes and *Dermacentor* and *Amblyomma* ticks as well as from several *Ixodes* species. However, the isolation of the bacterium from these ticks is not sufficient evidence to indicate that they transmit the disease to humans.

394. The answer is d. *(Howard, pp 707–708.)* While microsporidial infections are most common in patients with AIDS, microsporidia also cause infection, but rarely, in noncompromised hosts. Clinical presentations include seizure disorder, keratitis, and myositis. However, the most common infections in patients with AIDS involve the intestinal tract. There are four genera of microsporidia: *Encephalitozoon, Nosema, Enterocytozoon,* and *Pleistophora.* While a serologic test is available for *Encephalitozoon,* the usual laboratory detection method is a microscopic procedure employing a chromotropic stain. These organisms are tiny and differentiation from surrounding structures is difficult.

395–398. The answers are 395-c, 396-b, 397-d, 398-e. *(Levinson, pp 320–325.)* The life cycle of the medically important trematodes (or flukes) involves a sexual cycle in humans and an asexual cycle in snails. The schistosomes can penetrate the skin whereas *Clonorchis* and *Paragonimus* are ingested, usually in fish or seafood. These flukes can be easily differentiated morphologically by the appearance of the egg. Schistosome eggs have an identifiable spine, and both *Clonorchis* and *Paragonimus* eggs are operculated; that is, they have what appears to be a cover that opens. Serological tests are not useful. Many patients with schistosomiasis are asymptomatic, but disease may become chronic, resulting in malaise, diarrhea, and hepatosplenomegaly (an enlarged liver and spleen). *Clonorchis* infection usually causes upper abdominal pain but can also cause biliary tract fibrosis. Paragonimiasis is characterized by a cough, often with bloody sputum, and pneumonia. Praziquantel is the treatment of choice for these flukes.

399–402. The answers are 399-d, 400-a, 401-b, 402-c. *(Levinson, pp 325–331.)* It is not uncommon that repeated stool specimens do not reveal

the suspected parasite. Also, microscopic analysis of stool may not reveal parasite load when such data are necessary. For these reasons, other techniques are available to identify parasites as well as to quantitate them.

During sigmoidoscopy, a curette or suction device may be used to scrape or aspirate material from the mucosal surface. Cotton swabs should not be used. A direct mount of this material should immediately be examined for *E. histolytica* trophozoites, and then a permanent stain made for subsequent examination.

The Baermann technique may be helpful in recovering *Strongyloides* larvae. Essentially, fecal material is placed on damp gauze on the top of a glass funnel that is three-quarters filled with water. The larvae migrate through the damp gauze and into the water. The water may then be centrifuged to concentrate the *Strongyloides.*

Worm burdens may be estimated by a number of microscopic methods. While not often done, such procedures may provide data on the extent of infection or the efficacy of treatment of hookworms, *Ascaris,* or *Trichuris.* Thirty thousand *Trichuris* eggs per gram, 2000 to 5000 hookworm eggs per gram, and 1 *Ascaris* egg are clinically significant and suggest a heavy worm burden.

The diagnosis of giardiasis is usually made by detecting trophozoites and cysts of *G. lamblia* in consecutive fecal specimens. Alternatively, a gelatin capsule on a string (enterotest) can be swallowed, passed to the duodenum, and then retrieved after 4 h. The string is then examined for *Giardia.* A recent innovation is the introduction of an enzyme immunoassay (EIA) for *G. lamblia.* The EIA is more sensitive than microscopy, can be performed on a single stool specimen, and does not depend on the presence of entire trophozoites and cysts.

A cellophane tape swab is used to trap pinworms crawling out of the anus during the night. The tape is then examined microscopically for *Enterobius.*

403–407. The answers are 403-c, 404-a, 405-e, 406-b, 407-d. *(Levinson, pp 302, 306, 307, 320–335.)* All the diseases listed in the question have significant epidemiologic and clinical features. Toxoplasmosis, for example, is generally a mild, self-limiting disease; however, severe fetal disease is possible if pregnant women ingest *Toxoplasma* oocysts. Consumption of uncooked meat may result in either an acute toxoplasmosis or a chronic toxoplasmosis that is associated with serious eye disease. Most

adults have antibody titers to *Toxoplasma* and thus would have a positive Sabin-Feldman dye test.

Trichinosis most often is caused by ingestion of contaminated pork products. However, eating undercooked bear, walrus, raccoon, or possum meat also may cause this disease. Symptoms of trichinosis include muscle soreness and swollen eyes.

Although giardiasis has been classically associated with travel in Russia, especially St. Petersburg (Leningrad), many cases of giardiasis caused by contaminated water have been reported in the United States as well. Diagnosis is made by detecting cysts in the stool. In some cases, diagnosis may be very difficult because of the relatively small number of cysts present. Alternatively, an enzyme immunoassay may be used to detect *Giardia* antigen in fecal samples.

Schistosomiasis is a worldwide public health problem. Control of this disease entails the elimination of the intermediate host snail and removal of streamside vegetation. Abdominal pain is a symptom of schistosomiasis.

Visceral larva migrans is an occupational disease of people who are in close contact with dogs and cats. The disease is caused by the nematodes *Toxocara canis* (dogs) and *T. cati* (cats) and has been recognized in young children who have close contact with pets or who eat dirt. Symptoms include skin rash, eosinophilia, and hepatosplenomegaly.

408–412. The answers are 408-a, 409-d, 410-e, 411-b, 412-c. *(Howard, pp 656–659.) Trichomonas vaginalis,* an odd-looking protozoan, moves with a jerky, almost darting motion. Trichomoniasis, a bothersome vaginal infection, can be diagnosed by observing this organism in a wet mount of vaginal secretions. It may be washed out in the urine as well. *T. vaginalis* can be grown in special media and there are now several products available for direct detection of the organism.

Trichinella spiralis causes trichinosis, a parasitic disease that is usually mild and results in muscle pain and a mild febrile illness. However, fulminant fatal cases have been described. Humans, who are accidental hosts, become infected by ingesting cysts that are in the muscle of animals. Most infections still come from pork, although regulations on pig feeding have markedly reduced the incidence. Laboratory diagnosis is by serology or demonstration of the larvae in the muscle tissue.

Paragonimus westermani is a lung fluke. This trematode infects lung tissue and is seen not only in sputum but also in feces because infected

patients swallow respiratory secretions. Paragonimiasis is contracted by ingesting the metacercariae that are encysted in crabs or crayfish.

Giardia infection may be difficult to diagnose by stool examination as patients may shed the cysts intermittently. When symptoms persist and the stool examination is negative, then duodenal contents may be sampled directly with the enterotest. The patient swallows a gelatin capsule that contains a coiled string. The other end is attached to the patient's face. The gelatin capsule dissolves, and *Giardia* organisms, if present, adhere to the string within a 4-h period. The string is retrieved and examined microscopically. Alternatively, an enzymatic immunoassay can detect *Giardia* antigen directly in a single specimen of feces.

Babesia is a sporozoan parasite transmitted by the bite of *I. scapularis,* the same tick that carries *B. burgdorferi.* Reproduction of this parasite occurs in erythrocytes and may resemble *Plasmodium* species when blood smears are examined. *Babesia* is endemic in the northeastern United States, particularly in the islands of Massachusetts. Laboratory diagnosis is made by examining blood smears for this parasite or by detection of specific antibody. Babesiosis clinically resembles malaria.

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Immunology

Questions

DIRECTIONS: Each question below contains four or five suggested responses. Select the **one best** response to each question.

413. It is determined an infant suffers from Bruton's agammaglobulinemia. Which of the following pathogens will present the most serious threat to this child?

a. Measles virus
b. *Mycobacterium tuberculosis*
c. *Chlamydia trachomatis*
d. Varicella-zoster virus (VZV)

414. Megakaryocytes are minimally immunoresponsive; such cells are also known as

a. B lymphocytes
b. T lymphocytes
c. Cytokines
d. Interleukins
e. Platelets

415. One of the most remarkable aspects of the human immune system is its diversity, that is, the ability to recognize a wide range of antigens and to mount a specific antibody response. This is called *clonal selection*. At the cellular level, which of the following are primarily responsible for such specificity?

a. Cytotoxic T cells
b. Hypervariable regions in domains of B cells
c. The major histocompatibility complex
d. Specific T cell receptors
e. Memory cells

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416. A young girl has had repeated infections with *Candida albicans* and respiratory viruses since the time she was 3 months old. As part of the clinical evaluation of her immune status, her responses to routine immunization procedures should be tested. In this evaluation, the use of which of the following vaccines is contraindicated?

a. Diphtheria toxoid
b. *Bordetella pertussis* vaccine
c. Tetanus toxoid
d. BCG
e. Inactivated polio

417. A latent, measles-like viral infection and, presumably, a defect in cellular immunity is associated with which of the following diseases?

a. Progressive multifocal leukoencephalopathy (PML)
b. Multiple sclerosis (MS)
c. Creutzfeldt-Jakob disease
d. Subacute sclerosing panencephalitis (SSPE)
e. Epstein-Barr virus (EBV) infection

418. In humans, two closely linked genetic loci, each made up of two alleles, compose the histocompatibility locus A (HL-A). Paired first and second locus antigens are called *haplotypes*. The HL-A haplotypes (separated by a semicolon) of a child's parents are given below.

Father 3,25;7,12
Mother 1,3;8,9

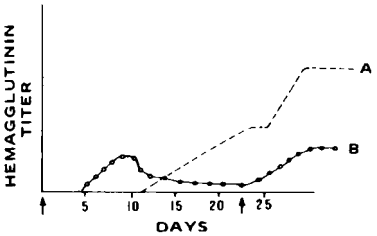
Assuming that no cross-over events have occurred, the child's histotype could be which of the following?

a. 1,3;7,8
b. 7,12;1,3
c. 3,3;7,9
d. 1,25;7,12
e. 3,25;7,12

419. The amounts of protein precipitated in a series of tubes containing a constant amount of antibody and varying amounts of antigen are presented below. In which tube is antigen-antibody equivalence obtained?

Tube	Antigen Precipitated (mg)	Protein (mg)
a.	0.02	1.1
b.	0.08	2.1
c.	0.32	3.1
d.	1.0	3.7
e.	2.0	2.9

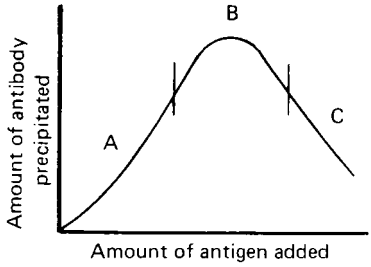
420. The graph below shows the sequential alteration in the type and amount of antibody produced after an immunization. (Inoculation of antigen occurs at two different times, as indicated by the arrows.) Curve A and curve B each represent a distinct type of antibody. The class of immunoglobulin represented by curve B has which of the following characteristics?



a. An estimated molecular weight of 150,000
b. A composition of four peptide chains connected by disulfide links
c. An appearance in neonates at approximately the third month of life
d. The human ABO isoagglutinin
e. A symmetric dipeptide

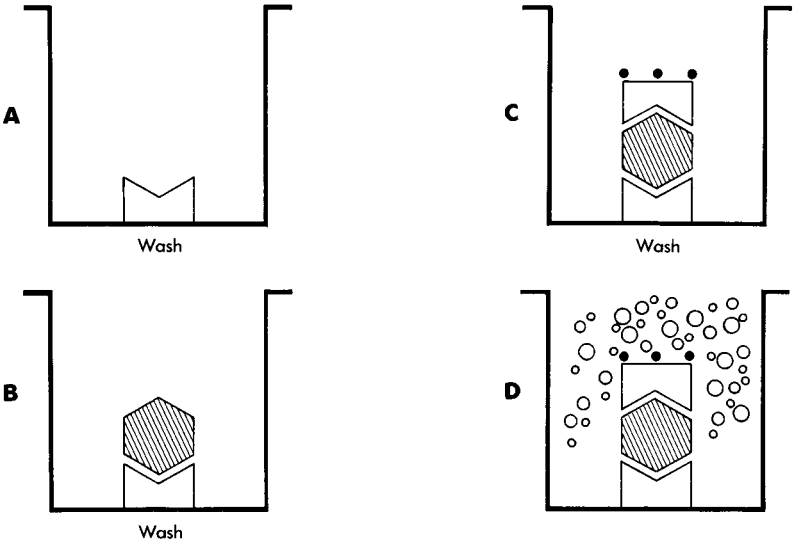
421. Which of the statements about the precipitin curve shown below is true?

a. In a multispecific system, a solution in zone B would have only an excess of antigen in the supernatant
b. In a monospecific system, a solution in zone B would contain only reacted antibody and antigen
c. A solution in zone A would be expected to have unreacted precipitable antigen in the supernatant
d. A solution in zone C would be expected to have both antigen and antibody in excess
e. A solution in zone C would be expected to have an excess of antibody in the supernatant



422. A widely used method for detecting either antigen or antibody in body fluids is known as ELISA (enzyme-linked immunosorbent assay). The figure below demonstrates an ELISA for detection of antigen. One of the problems with ELISA is nonspecific reactivity due to nonspecific antibody present in the reaction. Of the four steps depicted, A, B, C, and D, which one may be the major cause of nonspecificity?

a. B
b. A
c. D
d. C



Double antibody sandwich method of EIA for assay of antigen. A, antibody is adsorbed to surface. B, test solution containing antigen is added. C, enzyme-labeled specific antibody is added. D, enzyme substrate is added.

423. An Ouchterlony gel diffusion plate shows the reaction of a polyspecific serum against several antigen preparations. The center well in figure 1 contains polyspecific antiserum, first bleed; the center well in figure 2 contains polyspecific antiserum, second bleed; NS is normal saline. In this situation, cross-reaction can be recognized between antigen X and antigen

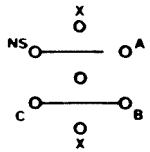


Figure 1

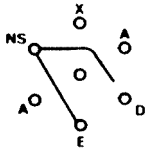


Figure 2

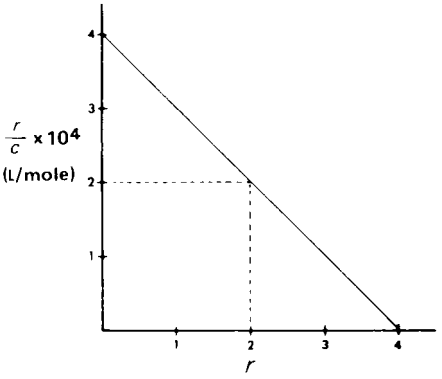
a. A
b. B
c. C
d. D
e. E

Questions 424–426

The Scatchard plot shown below represents the interaction of a hapten molecule with an immunoglobulin in an equilibrium dialysis apparatus. This interaction is defined by the equation

$$K = \left(\frac{r}{n \quad r} \right) c \qquad \text{or} \qquad \frac{r}{c} = Kn - Kr$$

(K is the intrinsic affinity constant, c is the free concentration of hapten, r is the number of hapten molecules bound per antibody molecule at c, and n is the antibody valence.)



424. The affinity constant for this system is

a. 1×10^{-4} L/mol
b. 1×10^{4} L/mol
c. 1×10^{4} L/mol
d. -4×10^{-4} L/mol
e. 16×10^{-4} L/mol

425. The antibody valence *n* is defined as the maximum number of ligand molecules able to be bound per antibody molecule. In the example presented, *n* equals

a. 1
b. 2
c. 3
d. 4
e. 10

426. The antibody species most likely to have been used in the experiment described is

a. IgA
b. IgD
c. IgE
d. IgG
e. IgM

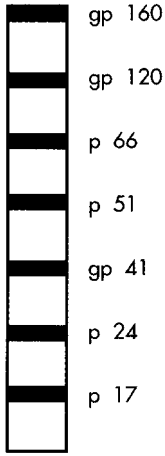
427. A 19-year-old college student develops a rash. She works part-time in a pediatric AIDS clinic. Her blood is drawn and tested for specific antibody to the chickenpox virus (varicella-zoster). Which of the following antibody classes would you expect to find if she is immune to chickenpox?

a. IgA
b. IgD
c. IgE
d. IgG
e. IgM

428. A 34-year-old male patient visits a physician with complaints of fatigue, weight loss, night sweats, and "swollen glands." The physician also observes that he has an oral yeast infection. Which of the following tests would most likely reveal the cause of his problems?

a. A test for CD8 lymphocytes
b. A human T-lymphotropic virus type I (HTLV-I) test
c. An HIV ELISA test
d. A test for infectious mononucleosis
e. A test for *Candida albicans*

429. The figure demonstrates a Western blot for HIV. Based on these results, and assuming a repeatedly reactive ELISA HIV screening test, your best course of action is to



a. Repeat the test immediately
b. Inform the patient that the test is falsely positive
c. Wait 6 weeks and repeat the test
d. Consider anti-HIV therapy
e. Order an HIV RNA test

430. A second patient makes an appointment. This patient, a 30-year-old male, requests a routine HIV test. The HIV ELISA was weakly positive and is repeated with the same results. The Western blot result is as shown in the preceding figure. The patient denies any risk factors for HIV. Which of the following is the most likely cause of a falsely positive HIV test?

a. A yeast infection
b. Test cross-reactivity with HTLV
c. Test cross-reactivity with Epstein-Barr virus
d. Naturally occurring HIV antibody
e. A recent "flu" shot

431. Patients with C5 through C9 complement deficiencies would be most likely to have which of the following infections?

a. AIDS
b. Meningococcal infection
c. Pneumococcal infection
d. Giardiasis
e. Histoplasmosis

432. There are at least 10 properties of cytokines. Which of the following is one of these characteristics?

a. Mitogenesis
b. B-cell lipids
c. Lipopolysaccharide (LPS) activation
d. T-cell differentiation
e. Hormonal antibody synthesis

433. Immunity may be natural or acquired. Which of the following best describes acquired immunity?

a. Increase in C-reactive protein (CRP)
b. Presence of natural killer (NK) cells
c. Complement cascade
d. Maternal transfer of antibody
e. Inflammatory response

434. A *hapten* is a nonimmunogenic small protein. Which of the following statements best describes haptens?

a. Haptens activate T cells
b. Penicillin is a hapten
c. Haptens do not react with specific antibody
d. Haptens bind the major histocompatibility complex (MHC)
e. Poison ivy is caused by a small protein that is not a hapten

435. The major role of T cells in the immune response includes which one of the following?

a. Recognition of epitopes presented with major histocompatibility complex molecules on all surfaces
b. Complement fixation
c. Phagocytosis
d. Production of antibodies

436. Which one of the following statements best describes immunoglobulin structure?

a. The amino acid sequence variation of the heavy chains is different than that observed in light chains
b. In humans, there are approximately twice as many Ig molecules with κ and λ chains
c. In the three-dimensional structure of Ig, there is little, if any, flexibility in the hinge region between the Fc and two Fab portions
d. IgM is a monomeric structure
e. Ig structural studies have been difficult because there is no readily available model protein

437. Specific immunological unresponsiveness is called *tolerance*. Which one of the following statements best describes immunological tolerance?

a. Immunologic maturity of the host does not play a major role
b. It occurs only with polysaccharide antigens
c. It is related to the concentration of antibody
d. It is best maintained by the presence of polysaccharide antigens
e. It is prolonged by administration of immunosuppressive drugs

438. It appears that HIV binds selectively to CD4 glycoproteins. Thus, HIV shows a selective infection with the destruction of helper T cells. Which of the following cells exhibit CD4 glycoprotein on their cell surface?

a. Macrophages
b. Polymorphonuclear leukocytes
c. Suppressor lymphocytes
d. Columnar epithelial cells
e. Squamous epithelial cells

439. Which one of the following statements best describes properties of interleukin 1 (IL-1)?

a. It is a macrophage-derived product
b. It does not activate B cells
c. It may stimulate cytoxic B cells
d. There is a single biologically active form
e. Its activity is histocompatibility-restricted

440. Interleukin 1 (IL-1) is a potent cytokine. It is best described by which one of the following statements?

a. Synthesis of IL-1 is inhibited in activated macrophages
b. It can be produced by natural killer cells
c. It exerts its effects on T and B cells as a costimulator
d. It is multimeric and consists of more than one protein
e. IL-6 has an inhibitory effect on IL-1

441. Survival of allografts is increased by choosing donors with few major histocompatibility complex (MHC) mismatches with recipients and by use of immunosuppression in recipients. Which one of the following procedures might be a useful measure of immunosuppression?

a. Administration of corticosteroids to recipient
b. Lymphoid irradiation of donor
c. Administration of immunoglobulin to recipient
d. Destruction of donor B cells
e. Destruction of donor T cells

442. Relative to the primary immunological response, secondary and later booster responses to a given hapten-protein complex can be associated with which one of the following?

a. Lower titers of antibody
b. Increased antibody affinity for the hapten
c. Decreased antibody avidity for the original hapten-protein complex
d. Maintenance of the same subclass, or idiotype, of antibody produced
e. Antibodies that are less efficient in preventing specific disease

443. Which one of the following hypotheses may be sufficient to explain nonprecipitation in antigen-antibody system?

a. The antigen has a multivalent determinant
b. The antigen has a single, nonrepeated determinant
c. The antibody has been cleaved to divalent Fab′ ligands
d. The antibody has been cleaved to divalent Fab'_2 ligands
e. The antibody has high affinity for the antigen

444. IgA antibody is the first line of defense against infections at the mucous membrane. It is usually an early specific antibody. Which of the following statements regarding IgA is not true?

a. Complement fixation tests for IgA antibody will be positive if specific IgA antibody is present
b. IgA is not found in saliva, therefore an IgA diagnostic test on saliva would have no value
c. IgA can be destroyed by bacterial proteases
d. IgA is absent in colostrum
e. IgA is a small molecule with a molecular weight of 30,000 kDa

445. Complement is a series of important host proteins which provide protection from invasion by foreign microorganisms. Which one of the following statements best describes complement?

a. Complement inhibits phagocytosis
b. Microorganisms agglutinate in the presence of complement but do not lyse
c. Complement plays a minor role in the inflammatory response
d. Complement protects the host from pneumococcal and *Haemophilus* infection through complement components C1, C2, and C4
e. Complement is activated by IgE antibody classes

Questions 446–450

The following five questions relate to immunoglobulins, IgG, M, A, D, and E.

446. Which immunoglobulin has no known function, but is present on the surface of B lymphocytes? It may function as an antigen receptor.

a. IgG
b. IgM
c. IgE
d. IgA
e. IgD

447. Which of the following is the immunoglobulin that is initially seen on the primary immune response? It is present as a monomer on B cell surfaces but as a pentamer in serum.

a. IgG
b. IgM
c. IgE
d. IgA
e. IgD

448. Which immunoglobulin mediates immediate hypersensitivity and is involved in immune response to parasitic infections?

a. IgG
b. IgM
c. IgE
d. IgA
e. IgD

449. Which immunoglobulin is the primary antibody in saliva, tears, and intestinal and genital secretions?

a. IgG
b. IgM
c. IgE
d. IgA
e. IgD

450. Which immunoglobulin is the predominant antibody in the secondary immune response? It has four subclasses.

a. IgG
b. IgM
c. IgE
d. IgA
e. IgD

451. IgM antibody (1:200) to *Borrelia burgdorferi* is associated with

a. Fifth disease
b. Susceptibility to chickenpox
c. Possible subacute sclerosing panencephalitis (SSPE)
d. Possible hepatitis B infection
e. Acute Lyme disease

452. Elevated IgG and IgM antibody titers to parvovirus suggest a diagnosis of

a. Fifth disease
b. Susceptibility to chickenpox
c. Possible subacute sclerosing panencephalitis (SSPE)
d. Possible hepatitis B infection
e. Acute Lyme disease

453. A negative varicella antibody titer in a young woman signifies

a. Fifth disease
b. Susceptibility to chickenpox
c. Possible subacute sclerosing panencephalitis (SSPE)
d. Possible hepatitis B infection
e. Acute Lyme disease

454. A patient has an increased antibody titer to delta agent. You would most likely suspect

a. Fifth disease
b. Susceptibility to chickenpox
c. Possible subacute sclerosing panencephalitis (SSPE)
d. Possible hepatitis B infection
e. Acute Lyme disease

455. A patient with neurological problems has an elevated cerebrospinal fluid (CSF) antibody titer to measles virus. You would most likely suspect

a. Fifth disease
b. Susceptibility to chickenpox
c. Possible subacute sclerosing panencephalitis (SSPE)
d. Possible hepatitis B infection
e. Acute Lyme disease

Questions 456–459

Infection with Epstein-Barr virus (EBV) results in the development of virus-specific antibodies. The pattern of these antibodies helps to stage the illness.

456. EBNA-Ab

a. Appears 2 weeks to several months after onset and is present more often in atypical cases of infectious mononucleosis
b. Appears 3 to 4 weeks after onset; titers correlate with severity of clinical illness
c. Arises early in the course of the illness; detectable titers persist a lifetime
d. Appears late in the course of the disease and persists a lifetime
e. Arises early in the course of the illness, and then titers fall rapidly

457. EA-EBV (anti-D) Ab

a. Appears 2 weeks to several months after onset and is present more often in atypical cases of infectious mononucleosis
b. Appears 3 to 4 weeks after onset; titers correlate with severity of clinical illness
c. Arises early in the course of the illness; detectable titers persist a lifetime
d. Appears late in the course of the disease and persists a lifetime
e. Arises early in the course of the illness, and then titers fall rapidly

458. EBV-VCA (IgG) Ab

a. Appears 2 weeks to several months after onset and is present more often in atypical cases of infectious mononucleosis
b. Appears 3 to 4 weeks after onset; titers correlate with severity of clinical illness
c. Arises early in the course of the illness; detectable titers persist a lifetime
d. Appears late in the course of the disease and persists a lifetime
e. Arises early in the course of the illness, and then titers fall rapidly

459. EBV-VCA (IgM) Ab

a. Appears 2 weeks to several months after onset and is present more often in atypical cases of infectious mononucleosis
b. Appears 3 to 4 weeks after onset; titers correlate with severity of clinical illness
c. Arises early in the course of the illness; detectable titers persist a lifetime
d. Appears late in the course of the disease and persists a lifetime
e. Arises early in the course of the illness, and then titers fall rapidly

Questions 460–464

Certain diseases are associated with a level of immune dysfunction (humoral, cellular, or both).

460. Ataxia-telangiectasia usually is associated with

	Humoral	Cellular
a.	Normal	Normal
b.	Normal	Deficient
c.	Deficient	Normal
d.	Deficient	Deficient
e.	Elevated	Elevated

461. Infantile X-linked agammaglobulinemia (Bruton's disease) is usually associated with

	Humoral	Cellular
a.	Normal	Normal
b.	Normal	Deficient
c.	Deficient	Normal
d.	Deficient	Deficient
e.	Elevated	Elevated

462. Swiss-type hypogammaglobulinemia is usually associated with

	Humoral	Cellular
a.	Normal	Normal
b.	Normal	Deficient
c.	Deficient	Normal
d.	Deficient	Deficient
e.	Elevated	Elevated

463. Thymic hypoplasia (DiGeorge's syndrome) is usually associated with

	Humoral	Cellular
a.	Normal	Normal
b.	Normal	Deficient
c.	Deficient	Normal
d.	Deficient	Deficient
e.	Elevated	Elevated

464. Wiskott-Aldrich syndrome is usually associated with

	Humoral	Cellular
a.	Normal	Normal
b.	Normal	Deficient
c.	Deficient	Normal
d.	Deficient	Deficient
e.	Elevated	Elevated

465. A xenograft is best described as a

a. Transplant from one region of a person to another
b. Transplant from one person to a genetically identical person
c. Transplant from one species to the same species
d. Transplant from one species to another species

466. An allograft is best described as a

a. Transplant from one region of a person to another
b. Transplant from one person to a genetically identical person
c. Transplant from one species to the same species
d. Transplant from one species to another species

467. An autograft is best described as a

a. Transplant from one region of a person to another
b. Transplant from one person to a genetically identical person
c. Transplant from one species to the same species
d. Transplant from one species to another species

468. An isograft is best described as a

a. Transplant from one region of a person to another
b. Transplant from one person to a genetically identical person
c. Transplant from one species to the same species
d. Transplant from one species to another species

Questions 469–471

Antigenic determinants on immunoglobulins are used to classify antibodies.

469. An isotype is characterized by

a. Determinant exposed after papain cleavage to an F(ab) fragment
b. Determinant from one clone of cells and probably located close to the antigen-binding site of the immunoglobulin
c. Determinant inherited in a Mendelian fashion and recognized by cross-immunization of individuals in a species
d. Heavy-chain determinant recognized by heterologous antisera
e. Species-specific carbohydrate determinant on the heavy chain

470. An allotype is characterized by

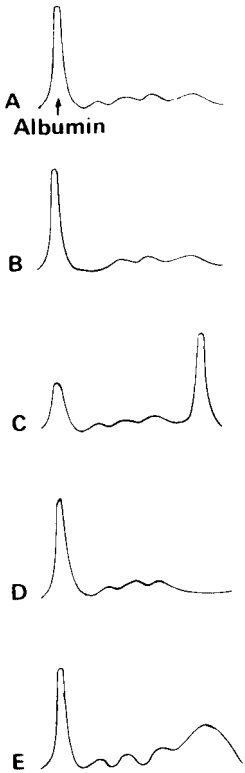
a. Determinant exposed after papain cleavage to an F(ab) fragment
b. Determinant from one clone of cells and probably located close to the antigen-binding site of the immunoglobulin
c. Determinant inherited in a Mendelian fashion and recognized by cross-immunization of individuals in a species
d. Heavy-chain determinant recognized by heterologous antisera
e. Species-specific carbohydrate determinant on the heavy chain

471. An idiotype is characterized by

a. Determinant exposed after papain cleavage to an F(ab′)2 fragment
b. Determinant from one clone of cells and probably located close to the antigen-binding site of the immunoglobulin
c. Determinant inherited in a Mendelian fashion and recognized by cross-immunization of individuals in a species
d. Heavy-chain determinant recognized by heterologous antisera
e. Species-specific carbohydrate determinant on the heavy chain

Questions 472–476

The following serum electrophoretic profiles (A–E) are associated with a variety of diseases. For each diagnosis given, choose the serum electrophoretic profile with which it is most likely to be associated.



472. α_1-Antitrypsin deficiency is associated with which one of the following patterns?

a. A
b. B
c. C
d. D
e. E

473. Multiple myeloma is associated with which one of the following patterns?

a. A
b. B
c. C
d. D
e. E

474. Swiss-type agammaglobulinemia is associated with which one of the following patterns?

a. A
b. B
c. C
d. D
e. E

475. Polyclonal hypergammaglobulinemia is associated with which one of the following patterns?

a. A
b. B
c. C
d. D
e. E

476. Which one of the following patterns would be seen in a normal person?

a. A
b. B
c. C
d. D
e. E

Questions 477–479

Complement-fixation (CF) testing is an important serological tool. One has to understand the conditions under which complement is bound and RBCs are lysed.

477. Anti-*Mycoplasma* antibody + complement + hemolysin-sensitized red blood cells (RBC) + anti-RBC antibody results in

a. Complement is bound, red blood cells are lysed
b. Complement is bound, red blood cells are not lysed
c. Complement is not bound, red blood cells are lysed
d. Complement is not bound, red blood cells are not lysed
e. Complement is not bound, red blood cells are agglutinated

478. Anti-*Mycoplasma* antibody + *Mycoplasma* antigen + complement + hemolysin-sensitized red blood cells + anti-RBC antibody results in

a. Complement is bound, red blood cells are lysed
b. Complement is bound, red blood cells are not lysed
c. Complement is not bound, red blood cells are lysed
d. Complement is not bound, red blood cells are not lysed
e. Complement is not bound, red blood cells are agglutinated

479. Anti-*Mycoplasma* antibody + *Mycoplasma* antigen + complement + hemolysin-sensitized red blood cells + anti-RBC antibody results in

a. Complement is bound, red blood cells are lysed
b. Complement is bound, red blood cells are not lysed
c. Complement is not bound, red blood cells are lysed
d. Complement is not bound, red blood cells are not lysed
e. Complement is not bound, red blood cells are agglutinated

Questions 480–484

Most, but not all, cases of hepatitis are caused by hepatitis A virus (HAV), hepatitis B virus (HBV), or non-A, non-B hepatitis virus (hepatitis C virus). While the laboratory diagnosis of HAV is usually accomplished by the detection of IgG and IgM antibodies to HAV, the diagnosis of HBV is more complex.

480. Finding IgG antibodies to core antigen, antibodies to e antigen, and antibodies to surface antigen reflects

a. Acute infection (incubation period)
b. Acute infection (acute phase)
c. Post infection (acute phase)
d. Immunization
e. HBV carrier state

481. Finding HBsAg positive and HBeAg positive reflects

a. Acute infection (incubation period)
b. Acute infection (acute phase)
c. Post infection (acute phase)
d. Immunization
e. HBV carrier state

482. Finding HBsAg positive, HBeAg positive, and IgM core antibody positive reflects

a. Acute infection (incubation period)
b. Acute infection (acute phase)
c. Post infection (acute phase)
d. Immunization
e. HBV carrier state

483. Finding HBsAg positive, no antibodies to HBsAg, and other tests variable reflects

a. Acute infection (incubation period)
b. Acute infection (acute phase)
c. Post infection (acute phase)
d. Immunization
e. HBV carrier state

484. Finding antibodies to HBsAg reflects

a. Acute infection (incubation period)
b. Acute infection (acute phase)
c. Post infection (acute phase)
d. Immunization
e. HBV carrier state

Questions 485–489

There are a variety of immunologic tests available for the detection of both antigen and antibody.

485. Which of the following tests combines features of gel diffusion and immunoelectrophoresis and is applicable only to negatively charged antigens?

a. Latex agglutination (LA)
b. Enzyme-linked immunosorbent assay (ELISA)
c. Enzyme multiplied immunoassay test (EMIT)
d. Counterimmunoelectrophoresis (CIE)
e. Coagglutination (COA)

486. Which of the following tests depends on the presence of protein A on certain strains of *Staphylococcus aureus*?

a. Latex agglutination (LA)
b. Enzyme-linked immunosorbent assay (ELISA)
c. Enzyme multiplied immunoassay test (EMIT)
d. Counterimmunoelectrophoresis (CIE)
e. Coagglutination (COA)

487. Which of the following tests is homogeneous immunoassay and is preferred for detection of low-molecular-weight substances?

a. Latex agglutination (LA)
b. Enzyme-linked immunosorbent assay (ELISA)
c. Enzyme multiplied immunoassay test (EMIT)
d. Counterimmunoelectrophoresis (CIE)
e. Coagglutination (COA)

488. Which of the following tests is used extensively to detect microbial antigens rapidly (5 min or less)? Inert particles are sensitized with either antigen or antibody.

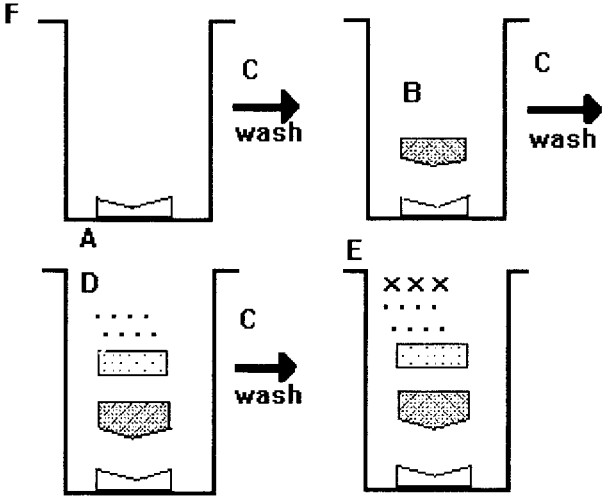
a. Latex agglutination (LA)
b. Enzyme-linked immunosorbent assay (ELISA)
c. Enzyme multiplied immunoassay test (EMIT)
d. Counterimmunoelectrophoresis (CIE)
e. Coagglutination (COA)

489. Which of the following tests is heterogeneous immunoassay? Its detection system is based on enzymatic activity.

a. Latex agglutination (LA)
b. Enzyme-linked immunosorbent assay (ELISA)
c. Enzyme multiplied immunoassay test (EMIT)
d. Counterimmunoelectrophoresis (CIE)
e. Coagglutination (COA)

Questions 490–494

The diagram presents the various steps (labeled A–F) of the enzyme immunoassay.



490. Failure of or improper methods for which step in the process will be the primary cause of high background color?

a. A
b. B
c. C
d. D
e. E
f. F

491. Where is unlabeled antibody attached if this enzyme immunoassay is intended for detection of antigen?

a. A
b. B
c. C
d. D
e. E
f. F

492. What is the location of the "solid phase"?

a. A
b. B
c. C
d. D
e. E
f. F

493. Addition of reagent at which step will cause color in the positive control well and reactive patient specimens?

a. A
b. B
c. C
d. D
e. E
f. F

494. What is the location of the patient specimen in the diagram?

a. A
b. B
c. C
d. D
e. E
f. F

495. Antistreptolysin titer of 400 international units (IU) indicates which one of the following diseases?

a. Chronic infectious mononucleosis
b. Primary syphilis
c. Scarlet fever
d. Primary atypical pneumonia
e. Immunity to rubella (German measles)

496. Hemagglutination inhibition titer (>1:20) suggests which one of the following diseases?

a. Chronic infectious mononucleosis
b. Primary syphilis
c. Scarlet fever
d. Primary atypical pneumonia
e. Immunity to rubella (German measles)

497. Reactive cold agglutinins suggests which one of the following diseases?

a. Chronic infectious mononucleosis
b. Primary syphilis
c. Scarlet fever
d. Primary atypical pneumonia
e. Immunity to rubella (German measles)

498. Epstein-Barr virus (EBV) VCA-IgG 1:80 and EBV antibody to early antigen (EA) 1:320 suggest which one of the following diseases?

a. Chronic infectious mononucleosis
b. Primary syphilis
c. Scarlet fever
d. Primary atypical pneumonia
e. Immunity to rubella (German measles)

499. A reactive rapid plasma reagin (RPR) test suggests which one of the following diseases?

a. Chronic infectious mononucleosis
b. Primary syphilis
c. Scarlet fever
d. Primary atypical pneumonia
e. Immunity to rubella (German measles)

500. A 31-year-old male patient complains of fatigue, yeast infection in his mouth, and enlarged lymph nodes under his arms. He said that he was involved in "high-risk" behavior 6 years ago while on a trip to eastern and southern Africa. He also indicated that his "HIV test" was negative. Which one of the following options would be most appropriate?

a. Initiate treatment for HIV disease
b. Order a test for human T cell leukemia virus (HTLV)
c. Repeat the test for HIV-1
d. Order an HIV test which would include antibodies to HIV-1 and HIV-2
e. Order an HIV-1 RNA PCR

Immunology

Answers

413. The answer is c. *(Mandell, p 1547.)* Bruton's agammaglobulinemia is a congenital defect that becomes apparent at approximately 6 months of age when maternal IgG is diminished. The child is unable to produce immunoglobulins and develops a series of bacterial infections characterized by recurrences and progression to more serious infections such as septicemia. Cell-mediated immunity is not affected and the child is able to respond normally to diseases that require this immune response for resolution.

414. The answer is e. *(Ryan, p 109.)* The primary constituent cells of the immune system are bone-marrow-derived lymphocytes (B cells) and thymus-derived lymphocytes (T cells). Cytokines are polypeptides that modulate the function of immunoresponsive cells, and interleukins are cytokines that are produced by mononuclear cells. Platelets appear not to be immunoresponsive and are involved in blood clotting.

415. The answer is b. *(Ryan, pp 110–111.)* The great heterogeneity in the B cell response is characterized by a wide variety of antigenic stimuli. The end result of this remarkable process is a set of very specific surface receptors on B lymphocytes. However, it is the hypervariable regions in the variable domain of these B cells that provide the amino acid residues that confer specificity by synthesis of surface immunoglobulin receptors. T cells, on the other hand, do not secrete immunoglobulins.

416. The answer is d. *(Levinson, pp 75–77.)* Recurrent severe infection is an indication for clinical evaluation of immune status. Live vaccines, including BCG attenuated from *Mycobacterium tuberculosis,* should not be used in the evaluation of a patient's immune competence because patients with severe immunodeficiencies may develop an overwhelming infection from the vaccine. For the same reason, oral (Sabin) polio vaccine is not advisable for use in such persons.

417. The answer is d. *(Ryan, p 472.)* Measles-like virus has been isolated from the brain cells of patients with subacute sclerosing panencephalitis (SSPE). The role of the host immune response in the causation of SSPE has been supported by several findings including the following: (1) progression of disease despite high levels of humoral antibody; (2) presence of a factor that blocks lymphocyte-mediated immunity to SSPE-measles virus in SSPE cerebrospinal fluid (CSF); (3) lysis of brain cells from SSPE patients by SSPE serum or CSF in the presence of complement (a similar mechanism could cause in vivo tissue injury).

Higher-than-normal levels of serum antibodies (Ab) to measles virus and local synthesis of measles Ab in CSF, as evidenced by the oligoclonal IgG, imply a connection between the virus and multiple sclerosis (MS). However, the other studies have implicated the other viruses. Several studies of cell-mediated hypersensitivity to measles and other viruses in MS have been done, but the results have been conflicting. Definite conclusions regarding defects in cellular immunity in this disease cannot be reached until further research is completed.

418. The answer is b. *(Levinson, p 376.)* In the question presented, the haplotypes of the father are 3,25 and 7,12 and the haplotypes of the mother are 1,3 and 8,9. (A haplotype is composed of one allele—antigen—from the one gene of a pair and one allele from the other gene.) Each child of this couple would have inherited one haplotype from each parent. Thus, possible offspring haplotypes are (1) 3,25; 1,3; (2) 3,25; 8,9; (3) 7,12; 1,3; and (4) 7,12; 8,9.

419. The answer is d. *(Levinson, pp 385–388.)* In tube d in the question presented, the maximum protein precipitate is observed. According to the rules governing precipitin reactions, maximum precipitation occurs at approximately antigen-antibody equivalence. In tubes a through c, antibody excess occurs; in tube e, antigen excess occurs.

420. The answer is d. *(Levinson, pp 344–349.)* The graph presented in the question exhibits hemagglutinating antibody responses to primary and secondary immunization with any standard antigen. Curve B represents the early response to primary immunization, which is chiefly an IgM response. Rechallenge elicits an accelerated response that mainly involves IgG and occurs 2 to 5 days after reimmunization. IgM has a molecular

weight of 900,000 and is a pentamer that the fetus can produce quite early in gestation.

421. The answer is b. *(Ryan, p 256–258.)* The ascending limb A of the precipitin curve presented in the question represents the zone of antibody excess; in this zone, the supernatant solution would contain unreacted antibody. On the descending limb C, or the antigen-excess zone, the supernatant solution contains excess free antigen. In a monospecific system, B designates the region of maximum precipitation and the supernatant solution is free to precipitate antibody and antigen. In a complex multispecific system, excess antigen or antibody molecules may be present at the point of maximum precipitate formation because the optimal quantity of each antigen may be different.

422. The answer is b. *(Ryan, p 235.)* ELISA (enzyme-linked immunosorbent assay) methods can be used to detect either antigens or antibodies. If antibody is to be detected, then antigen is initially bound to the plate (see A in the diagram presented with the question). If antigen is to be detected, then specific antibody is bound to the solid phase. The bound antigen and antibody then "captures" the analyte to be detected. One of the major causes for high background in ELISA tests is the failure to wash off unbound antigen or antibody (see B in the diagram presented with the question).

423. The answer is a. *(Levinson, p 373.)* In the Ouchterlony agar-gel diffusion test, an antigen and a series of antibodies (or an antibody and a series of antigens) are allowed to diffuse toward each other. At the zone of optimal proportions of the reactants, a precipitin line occurs. Cross-reactions between antigens or antibodies tested can be detected by (1) a shortening of the major precipitin band contiguous to the cross-reacting substance, or (2) the identity of precipitin reaction between the two cross-dressing substances. The figures presented in the question illustrate both types of cross-reaction. In the first bleed pattern shown in the question, cross-reaction between antigen X and antigen A is recognizable only by a shortening of the precipitin band between the center well and X on the A well side (relative to the band going directly into the normal saline well). In the second bleed pattern, full cross-reaction of X and A is apparent. No other cross-reactions are seen.

424. The answer is c. *(Davis, pp 249–252.)* In a Scatchard plot, the slope of the line is equal to $-K$. As shown in the graph presented with the question, the slope ($r/c \div r$) is $-[(2 \times 10^4 \text{ L/mol}) \div 2] = -1 \times 10^4$ L/mol. Thus, K equals 1×10^4 L/mol.

425. The answer is d. *(Davis, pp 249–252.)* In the graph presented with the question, as r approaches 4, r/c approaches 0, and consequently, c approaches infinity. In general, the x-intercept (that is, $r/c = 0$) gives the number of ligand-binding sites at maximal saturation. In the example described, this maximum number of ligand molecules able to be bound per antibody molecule—or the antibody valence—is 4. Antibody valence also can be calculated from the equation given; that is, if $r/c = 2 \times 10^4$ L/mol, $r = 2$, and $K = 1 \times 10^4$ L/mol, then $n = [(r/c + Kr) \div K] = [(2 \times 10^4 \text{ L/mol} + 2 \times 10^4 \text{ L/mol}) \div 1 \times 10^4 \text{ L/mol}] = 4$.

426. The answer is a. *(Levinson, pp 366–368.)* Secretory IgA is a tetravalent dimer and thus would have an antibody valence of 4 (calculated in the previous question). IgG and IgE are divalent immunoglobulins. IgM is a pentavalent or decavalent, depending on the experimental conditions.

427. The answer is d. *(Ryan, p 115.)* The initial response to a new infection is with an IgM class antibody. IgM develops quickly and usually disappears within a few months. The secondary response is IgG and reflects the patient's immune status or, in the case of chickenpox, a vaccination given.

428–430. The answers are 428-c, 429-d, 430-e. *(Ryan, pp 550–555.)* A male patient with the presentation as outlined in question 428 (fatigue, weight loss, and lymphadenopathy) must be tested for antibodies to HIV. While other antibody tests may be relevant after the primary diagnosis, they must be considered after HIV is ruled out. Certainly, infectious mononucleosis is a possibility, but its occurrence in this age group is not as frequent as HIV. Patients are tested first by an ELISA screening test. If this test is positive (X2), then a confirmatory Western blot is performed. A Western blot separates the immune response into antibody production for specific components of the virus, that is, envelope, gag, and so forth. The following table shows the various bands that could be seen on a widely used Western blot and their identification by specific antigen source. There

are at least three schemes for interpreting Western blots. Assuming technical competence in the laboratory, one of the more common reasons for falsely positive ELISAs and Western blots is an influenza vaccination within the past few months. A rare patient may have antibody to the cell line used to grow virus. Unlike Lyme disease, there is no reported cross-reactivity with Epstein-Barr virus (EBV) or HTLV. There appears to be no naturally occurring antibody to retroviruses.

Antigen	Source
gp 160	env gene product
gp 120	env fragment
gp 41	transmembrane fragment
gp 31	
gp 51	pol gene product
p 66	
p 24	core protein (gag)

Abbreviations: gp, glycoprotein; p, protein; env, envelope; pol, polymerase.

431. The answer is b. *(Howard, pp 16–17.)* Patients with complement deficiencies such as C5 through C9, which form the membrane attack complex (MAC), are predisposed to disseminated meningococcal disease. These patients may also be susceptible to gonococcal infection. There appears to be no disposition to AIDS or to fungal, parasitic, or pneumococcal infections.

432. The answer is a. *(Ryan, p 109.)* There are at least 10 functions of the known cytokines, including mitogenesis, lymphocyte activation, pyrogenesis, lymphocyte proliferation, and T-cell differentiation. Not all cytokines (such as interleukins) are responsible for all of these functions. Cytokines do not activate LPS, but LPS may activate macrophages.

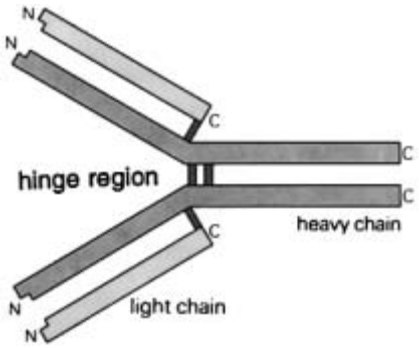
433. The answer is d. *(Levinson, pp 42–47.)* Natural immunity is nonspecific. The description of natural immune functions described are not specific for a certain antigen. For example, certain proteins such as C-reactive protein (CRP) are acute-phase reactants. While elevated CRP is seen in infection, it is

not disease-specific. Maternal transfer of antibody, however, is passive but still confers specific immunity. It is termed *acquired* immunity.

434. The answer is b. *(Levinson, p 343.)* While haptens react with antibodies, they are not immunogenic because they do not activate T cells and cannot bind the major histocompatibility complex (MHC). Haptens are significant in disease; penicillin is a hapten and can cause severe life-threatening allergic reaction. Catechols in the oils of poison ivy plants are haptens and cause a significant skin inflammatory response.

435. The answer is a. *(Ryan, pp 110–111.)* T cells do not synthesize antibody; that is the task of B cells. Recognition of certain epitopes, lymphokine production, and eradication of "foreign cells" are all functions of T cells. One of the best-recognized T cells is the CD4 cell. The importance of CD4 cells to the immune response is demonstrated by the effects of a specific inhibition of CD4 functions, that is, human immunodeficiency virus (HIV).

436. The answer is b. *(Ryan, pp 115–122.)* Following is a schematic figure of Ig. Note that each peptide chain is drawn as a continuous line and attachments between heavy and light chains are noted by solid bars. There appears to be considerable flexibility in the hinge region between the Fc and the two Fab portions of the molecule. This allows the molecule to assume either a T shape or a Y shape. Myeloma proteins have been widely used for Ig structural studies.



The basic immunoglobulin structure. The unit consists of two identical light polypeptide chains and two identical heavy polypeptide chains linked together by disulphide bonds.

437. The answer is e. *(Levinson, pp 401–402.)* Whether an antigen will induce tolerance rather than an immunologic response is largely determined by immunologic maturity of the host, structure, dose of antigen, and administration of immunosuppressive drugs. Tolerance is best maintained by the presence of low concentrations of antigen. T cells become tolerant more readily than B cells.

438. The answer is a. *(Levinson, p 348.)* Except squamous epithelial cells, all of the cells listed exhibit CD4 glycoprotein on their cell surface, although at lower levels, than do helper T cells. This explains, in part, how HIV infection may be neurotropic. Because of the low levels of CD4 glycoprotein, these cells, as well as colon epithelial cells, are susceptible to HIV infection. Suppressor lymphocytes have a CD8 glycoprotein determinant.

439. The answer is a. *(Ryan, pp 107–109.)* Interleukin 1 is a protein produced by macrophages that has three biologically active forms: IL-α, β, and γ. Its functions include activation of B cells and stimulation of helper and cytotoxic T cells. Its activity is not histocompatibility-restrained.

440. The answer is b. *(Levinson, pp 345–359.)* Interleukin 1 (IL-1) is produced by a variety of cells. Primarily, it is produced by activated macrophages or monocytes, although it can also be produced by activated B cells, keratinocytes, skin-layer hairy cells, and natural killer cells. IL-1 acts synergistically with IL-6 to stimulate production of IL-2. Human IL-1 consists of α and β forms, or two different proteins. They have limited similarity of amino acid sequence, and the β form is more abundant as a serum protein.

441. The answer is a. *(Davis, pp 466–467.)* Allograft rejection is primarily a T-cell response to foreign tissue. The corticosteroids reduce inflammatory response and are generally administered by cytotoxic drugs, such as cyclosporine. Lymphoid irradiation is usually done so that the bone marrow is shielded. This removes lymphocytes from lymph nodes and spleen while allowing the patient to have the capacity to regenerate new T and B cells. Likewise, antilymphocyte globulin will destroy the recipient's lymphocytes, especially T cells. Destruction of donor B cells and T cells would not play a role in the immunosuppression of the graft recipient. In graft crises, monoclonal antibody to CD3 is sometimes given. This targets mature T lymphocytes for destruction.

442. The answer is b. *(Davis, pp 869, 893–894.)* With repeated immunization, higher titers of all antibodies are observed, and, as priming is repeated, the immune response recruits B cells of progressively greater affinity. The affinity of antibody for a hapten-protein complex rises, cross-reactivity also rises, and the response becomes wider in specificity. As the number of antigenic sites detected per reacting particle increases, the avidity increases. In addition to shifts in the class of immunoglobulin synthesized in response to an antigen (IgM to IgG), shifts also may occur in the idiotype of antibody.

443. The answer is c. *(Davis, pp 256–261.)* Neither monovalent antigen nor monovalent antibody (Fab:) can form a precipitin lattice. An antigen molecule containing closely repeating antigen determinants (e.g., a polysaccharide or a multichained polymeric protein), can bind antibody to two determinants on a single particle; this "monogamous bivalency" inhibits precipitation. Fab'_2 divalent antibodies can precipitate antigens, though they lack Fc portions.

444. The answer is c. *(Howard, pp 118–119.)* Each secretory IgA molecule has a molecular weight of 400,000 and consists of two H2L2 units and one molecule each of J chain and secretory component. Some IgA exists in serum as a monomer H2L2 with a molecular weight of 160,000. Some bacteria, such as *Neisseria,* can destroy IgA1 by producing protease. It is the major immunoglobulin in milk, saliva, tears, and colostrum. IgA does not fix complement, so one would anticipate that a complement fixation test would not be useful for IgA antibody.

445. The answer is d. *(Howard, p 17.)* Both IgG and IgM activate complement by the classic pathway, while IgA activates it by the alternative pathway. Neither IgD nor IgE can activate complement. Complement is a system of several proteins that is activated by either an immune or a nonimmune pathway. Both of these pathways result in the production of many biologically active components that cause cell lysis and death.

446–450. The answers are 446-e, 447-b, 448-c, 449-d, 450-a. *(Levinson, pp 363–372.)* IgG antibody provides an "immune history." That is, IgG antibody persists in most people and indicates the antigens to which they have been exposed. IgG is not formed early in infection but is a sec-

ondary response arising weeks to months after antigenic challenge. IgG also has a built-in memory. Even people with very low levels of specific IgG will respond to an antigen challenge with an IgG response.

IgM antibody, in contrast, arises early in infection and then disappears within a couple of months. IgM is intravascular and does not cross the placental barrier. For this reason, infants with specific IgG responses to disease must be tested for IgM to determine whether their immune systems have produced antibody or whether the test was positive because of passively transferred IgG.

IgA antibody is involved in local immunity at the level of the mucous membrane. IgA antibody also arises early in disease. IgA antibody is short-lived and will disappear similarly to IgM.

IgE antibody is characteristically seen in parasitic infections, particularly worm (helminth) infections because of the attraction of eosinophils to the site of the infestation. Certain allergies are due to excessive production of IgE.

IgD antibody consists of two light chains and two heavy chains. Its role is not known but can be found on the surface of lymphocytes where it may act as a surface receptor.

IgG is susceptible to proteolytic enzymes, which may explain why it is present in such low levels in serum.

451–455. The answers are 451-e, 452-a, 453-b, 454-d, 455-c. *(Howard, pp 535–537, 754, 755, 789–791.) Borrelia burgdorferi,* the causative agent of Lyme disease, elicits an acute antibody response. IgM appears within days to a few weeks following tick bite, and IgG appears a few weeks later. IgG persists, IgM does not. Cross-reactions occur with other treponemes.

Fifth disease is a viral exanthem commonly seen in children 8 to 12 years old. Children are ill for a few days but recover without incident. Unfortunately, if a pregnant female acquires the disease in the first trimester of pregnancy, the fetus is at risk. The causative agent is thought to be a parvovirus (parvovirus B 19).

Adults with no titer to varicella (VZV) are at risk for acquisition of chickenpox. If they are health care workers, there is additional risk in transmitting VZV to immunodeficient children. Antibodies to VZV are readily detected by both enzyme immunoassay (EIA) and fluorescent-antibody (FA) techniques.

Delta agent is a recently discovered antigen associated with HBsAg. Its presence usually correlates with HBsAg chronic carriers who have chronic

active hepatitis. EIA and radioimmunoassay (RIA) tests are available to detect antibodies to delta agent.

SSPE is thought to be caused by a measles-related virus present in the central nervous system. Most SSPE patients show elevated measles virus antibodies in serum and CSF. In patients with multiple sclerosis (MS), lower CSF antibody titers have been observed, suggesting a possible etiologic role for measles virus in MS.

456–459. The answers are 456-d, 457-b, 458-c, 459-e. *(Ryan, pp 513–517.)* Epstein-Barr virus (EBV), a member of the human herpesvirus group, has been established as the causal agent of heterophil-positive and heterophil-infectious mononucleosis. The diagnosis of infectious mononucleosis can be made in 80 to 90% of cases by demonstration of heterophil antibodies. In the heterophil-negative cases and for atypical infections, determination of specific antibodies to EBV are useful in establishing the diagnosis. The development of IgM antibodies to the viral capsid antigen (EBV-VCA [IgM] Ab) can be used for specific diagnosis of a current or recent infection. They arise early in the disease and persist for only 4 to 8 weeks.

On the other hand, many adults have been exposed to EBV and maintain a low level of IgG in response to this virus. A titer of greater than 1:640 is usually diagnostic.

Antibodies to the early antigen of EBV (EA-EBV) show two distinct patterns of fluorescence-diffuse staining of both nuclei and cytoplasm (anti-D) and staining of cytoplasmic aggregates (anti-R). Anti-D titers appear 3 to 4 weeks after onset and are present in 70% of EBV-induced mononucleosis. Titers correlate with the severity of clinical illness and disappear after recovery. Anti-R titers appear two weeks to several months after onset and are rarely seen in cases of infectious mononucleosis. They are detectable in atypical cases and remain so for up to two years.

Antibodies to the nuclear antigen of EBV (EBNA-Ab) appear three to four weeks after onset and persist for life. They are useful in assessing recent infection if patients are VCA-positive, EBNA-negative, and then become EBNA-positive.

460–464. The answers are 460-d, 461-c, 462-d, 463-b, 464-d. *(Levinson, pp 408–413.)* Immunodeficiency disorders can be categorized according to whether the defect primarily involves humoral immunity

(bone marrow–derived, or B lymphocytes) or cellular immunity (thymus-derived, or T lymphocytes) or both. Swiss-type hypogammaglobulinemia, ataxia-telangiectasia, the Wiskott-Aldrich syndrome, and severe combined immunodeficiency disorders all involve defective B-cell and T-cell function. Infantile X-linked agammaglobulinemia is caused chiefly by deficient B-cell activity, whereas thymic hypoplasia is mainly a T-cell immunodeficiency disorder.

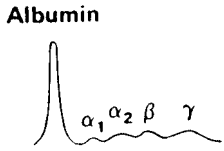
465–468. The answers are 465-d, 466-c, 467-a, 468-b. *(Levinson, pp 377–380.)* Transplantation from one region of a person to another region of that same person is an *autograft* and has the best chance of succeeding. When a transplant is done between monozygotic twins, it is an *isograft* and has a complete MHC compatibility and a good chance of success. *Allografts* are between members of the same species, and *xenografts* are between members of different species. Both of these transplants have a high rate of rejection unless immunosuppression accompanies the transplant.

469–471. The answers are 469-d, 470-c, 471-b. *(Levinson, pp 370–371.)* Isotypes are determined by antigens of the immunoglobulin classes found in all individuals of one species. In addition to heavy-chain isotypes of IgA, IgD, IgE, IgG, and IgM, two light-chain isotypes exist for κ and λ chains.

Allotypes are differentiated by antigenic determinants that vary among individuals within a species and are recognized by cross-immunization of individuals in a species. Allotypes include the Gm marker of IgG and the Inv marker of light chains.

Idiotypes are antigenic determinants that appear only on the Fab fragments of antibodies and appear to be localized at the ligand-binding site; thus, anti-idiotype antisera may block reactions with the appropriate hapten. The carbohydrate side chains of immunoglobulins are relatively nonimmunogenic. New determinants may be exposed after papain cleavage of immunoglobulins, but these determinants are not included in the classification of the native molecule.

472–476. The answers are 472-b, 473-c, 474-d, 475-e, 476-a. *(Davis, pp 278–282.)* Electrophoresis of human serum proteins identifies five distinct types: albumin, α_1-proteins, α_2-proteins, β-proteins, and γ globulins. A normal electrophoretic profile appears next page.



Many human diseases can be diagnosed, at least in part, on the basis of abnormal electrophoresis profiles. For example, absence of the second peak (α_1) is compatible with a diagnosis of α_1-antitrypsin deficiency in symptomatic persons. A sharp and high γ peak indicates the presence of a monoclonal gammopathy, such as multiple myeloma; on the other hand, a γ peak that is diffusely elevated points to polyclonal hypergammaglobulinemia. Complete absence of the γ peak is associated with Swiss-type agammaglobulinemia.

477–479. The answers are 477-c, 478-b, 479-b. *(Ryan, pp 236–237.)* The complement-fixation (CF) test is a two-stage test. The first stage involves the union of antigen with its specific antibody, followed by the fixation of complement to the antigen-antibody structure. In order to determine whether complement has been "fixed," an indicator system must be employed to determine the presence of free complement. Free complement binds to the complexes formed when red blood cells (RBCs) are mixed with anti-RBC antibody; this binding causes lysis of the cells. Complement that has been "fixed" before addition of red blood cells and anti-RBC antibody cannot cause lysis.

480–484. The answers are 480-c, 481-a, 482-b, 483-e, 484-d. *(Howard, pp 829–830.)* The following table presents the patterns of hepatitis B virus serologic markers observed in various stages of infection with HBV. The diagnosis of HBV infection is usually based on three tests: hepatitis B surface antigen, antibodies to surface antigen, and antibodies to core antigen. Tests are available, however, for e antigen and antibodies to e antigen. A variety of testing methods are available and include enzyme immunoassay, radioimmunoassay, hemagglutination, latex agglutination, and immune adherence. The delta agent has recently been described. The delta agent exacerbates infection with HBV, apparently in a synergistic manner. Commercial tests are now available for the delta agent.

Interpretation	Serologic Markers					
	HBsAg	Anti-HBeAg	IgM Anti-HBc	Total Anti-HBc	Anti-HBe	HBs
Acute infection						
Incubation period	+*	+*	–	–	–	–
Acute phase	+	+	+	+	–	–
Early convalescent phase	+	–	+	+	+	–
Convalescent phase	–	–	+	+	+	–
Late convalescent phase	–	–	–†	+	+	+
Long past infection	–	–	–	+‡	+ or –	+‡
Chronic infection						
Chronic active hepatitis	+§	+ or –	+ or –	+§	+ or –	–§
Chronic persistent hepatitis	+¶	+ or –	+ or –	+	+ or –	–
Chronic HBV carrier state	+¶	+ or –	+ or –	+	+ or –	–
HBsAg immunization	-	-	-	-	-	+

*HBsAg and HBeAg are occasionally undetectable in acute HBV infection.
†IgM anti-HBc may persist for over a year after acute infection when very sensitive assays are employed.
‡Total anti-HBc and anti-HBs may be detected together or separately long after acute infection.
§HBsAG-negative chronic active hepatitis may occur where total anti-HBc and anti-HBs may be detected together, separately, or not at all.
¶HBsAg-negative chronic persistent hepatitis and chronic HBV carriers have been observed.

485–489. The answers are 485-d, 486-e, 487-c, 488-a, 489-b. *(Ryan, p 238.)* Of the many methods available for antigen and antibody detection, LA, ELISA, EMIT, CIE, and COA are the most widely used. Latex agglutination (LA) employs latex polystyrene particles sensitized by either antibody or antigen. LA is more sensitive than CIE and COA but slightly less sensitive than either RIA or EIA. LA has been used to detect *Haemophilus influenzae, Neisseria meningitidis,* and *Streptococcus pneumoniae* antigens in cerebrospinal fluid. LA has also been used for detection of cryptococcal antigen. Most recently, LA has been widely used for rapid detection of group A streptococcal antigen directly from the pharynx. The test is rapid (5 minutes), sensitive (approximately 90%), and specific (99%).

Coagglutination (COA), also an agglutination test, is slightly less sensitive than LA but less susceptible to changes in environment (e.g., temperature). Most strains of coagulase-positive staphylococci have protein A in their cell wall. Protein A binds the Fc fragment of microbial antigens in body fluids. COA has also been used to rapidly type or group bacterial isolates.

Enzyme immunoassays (EIAs) can be either homogeneous (EMIT) or heterogeneous (ELISA). EMIT has been used primarily for assays of low-molecular-weight drugs. Its primary use in microbiology has been for assays of aminoglycoside antibiotics. EIAs vary as to the solid support used. A variety of supports can be used, such as polystyrene microdilution plates, paddles, plastic beads, and tubes. The number of layers in the antibody-antigen sandwich varies; usually as additional layers are added, detection sensitivity is increased. The two most common enzymes are horseradish peroxidase (HRP) and alkaline phosphatase (AP). β-galactosidase has also been employed. Orthophenylene diamine is the most common substrate for HRP and p-nitrophenyl phosphate for AP. Because EIAs are usually read in the visible color range, the tests can be read qualitatively by eye or quantitatively by machine.

Counterimmunoelectrophoresis (CIE) was originally used for "Australia antigen" (HBsAg) but was soon replaced by RIA. For a decade, CIE was used to detect antigens in body fluids, CIE is not an easy technique. Its success depends on the control of many variables, including solid support, voltage, current, buffer, affinity and avidity of antibodies, charge on the antigen, and time of electrophoresing.

490–494. The answers are 490-c, 491-a, 492-f, 493-e, 494-b. *(Howard, pp 122–125.)* The enzyme immunoassay (EIA, ELISA) has become a common method for the detection of either antibody or antigen in a patient specimen. The technique is based on building a "sandwich." For example, the following sandwich is made on what is called the *solid phase*. The solid phase is usually a plastic microtiter plate but can be a plastic paddle or even a nitrocellulose membrane. First, whole *Toxoplasma* organisms or purified antigenic components of *Toxoplasma* are added to the plate and the plate is washed off. Failure of one or more of the washing steps or inadequate washing usually causes high background color in the developed plate.

The *Toxoplasma* antigen-antibody complex must be detected by the addition of a second antibody to which is linked an enzyme such as horseradish peroxidase or alkaline phosphatase. The nature of this second anti-

body is dependent on whether one wishes to measure IgG or IgM. If the test is for IgG, then the second antibody is anti-human IgG conjugated to an enzyme. Following another wash cycle, the enzyme substrate is added to the plate and color develops in those wells where the sandwich is complete. If the patient's serum does not contain specific antibody, then the sandwich is not completed and there is no development of color. If the EIA is for detection of antigen, then the layers of the sandwich are as follows:

Specific antibody
Patient specimen (contain antigen)
Enzyme-labeled antibody specific for the antigen
Enzyme substrates

There are many variations of the test using a variety of antibodies, indicators such as fluorescence, and magnetic beads as solid phases. EIA is more sensitive than agglutination methods or complement fixation and slightly less sensitive than radioimmunoassay.

495–499. The answers are 495-c, 496-e, 497-d, 498-a, 499-b. *(Howard, pp 264–266, 491–500, 534–535, 793–795, 819–821.)* Scarlet fever is usually a clinical diagnosis subsequent to streptococcal pharyngitis. Acute group A streptococcal infections result in elevated antibody titers to streptolysin (ASO), DNase B, NADase, and hyaluronidase, all soluble products of streptococcal growth.

Rubella immune status tests are usually done by hemagglutination inhibition (HI), enzyme immunoassay (EIA), or latex agglutination. Reactive HI titers are 1:10 or greater. IgM tests for rubella are often necessary in congenital infection in order to separate maternal from fetal antibodies.

Mycoplasma pneumoniae causes primary atypical pneumonia. Although physicians rely on the presence of cold agglutinins (CA) for diagnosis, CA may be negative in up to 50% of cases. With symptoms of pneumonia, a positive CA is reliable. A complement-fixation (CF) test for *M. pneumoniae* is indicated when CA is negative. Isolation of *M. pneumoniae* is time-consuming (1 to 3 weeks) and not practical in most circumstances.

Infectious mononucleosis (IM) may be suspected clinically but it is confirmed serologically. The heterophil antibody test, however, may be negative in up to 15% of adults and 35 to 40% of children. Because IM is caused by Epstein-Barr virus (EBV), a specific test for viral capsid antigen (VCA) of EBV is indicated when heterophil tests are negative. Acute IM is character-

ized by a VCA-IgM titer, and no VCA-IgG antibody or EBNA. Chronic EBV disease causes elevated VCA-IgG titers as well as high EA antibody titers.

In the rapid plasma reagin (RPR) tests, the patient's serum is mixed on a card with RPR antigen and sensitized charcoal particles. If antibody is present, the particles clump. The RPR is more sensitive than the VDRL test, but as with the VDRL test, false positives may occur in 15 to 20% of the positive RPR results. All positives must be confirmed with a specific treponemal test for syphilis such as the fluorescent treponemal antibody-absorption test (FTA-ABS).

500. The answer is d. *(Raoult, pp 484–485.)* HIV-2 disease is very rare in the United States. However, HIV-2 is present in Africa, the Far East, and some parts of the Caribbean area. Many of the screening tests for HIV-1 will not detect antibodies to HIV-2. Either a separate HIV-2 antibody test or a combination HIV-1/2 is necessary. While HTLV disease is also seen in the same geographic areas, the symptoms are more akin to HIV disease. While an HIV-1 RNA PCR is a useful test for monitoring the results of HIV therapy, it is not approved for diagnosis nor will it detect HIV-2 nucleic acid.

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Index

A
Acanthamoeba, 179, 199–200
Actinomyces, 75, 102
  A. israelli, 61, 82, 92, 105
  A. viscosus, 82, 105
Acute hemorrhagic conjunctivitis (AHC), 9, 35
Adenosine triphosphate (ATP), 111, 130
Adenovirus, 13, 20, 24, 27, 31, 39, 45, 48, 50, 51*t*
α-hemolytic streptococci, 81, 104
AIDS:
  progression to, 1, 5, 32
  triple therapy for, 6, 33
  (*See also* HIV)
Ajellomyces:
  A. capsulata, 163, 173
  A. dermatitidis, 163
Allograft, 229, 250
  rejection, 223, 246
Allotype, 230, 250
Alphavirus, 13, 39
Amdinocillin, 125, 137
Amebae, 190, 190*f*, 203
  intestinal, 193, 205
Amphotericin, 125, 137
Amplicons, 117, 134
Antibiotics:
  β-lactam, 2
  broad-spectrum, 124–125, 136–137
Antigen-antibody precipitation, 213, 213*t*, 223, 241, 247
Antimicrobial agents, 2
Arbovirus, 7, 34
Arthroderma van breuseghemii, 162, 173
Ascaris, 195, 207
Aspergillus, 159–161, 169–172, 175
  A. fumigatus, 166
Astrovirus, 28, 51*t*
Ataxia-telangiectasia, 228, 250
Atypical lymphocytosis, 20, 45
Autograft, 230, 250
α1–Antitrypsin deficiency, 232, 251

B
Babesiosis, 2, 177, 177*f*, 198–199, 209
Bacillus anthracis, 128, 139
Bacteria:
  components of, 127, 138
  DNA transfer in, 120, 135
  fimbriae function in, 112, 131
  growth curves of, 113–114, 131–132
  isolation of, 79, 103–104
  P/O ratio in, 111, 130
  recognition of abnormal, 80, 104
  virulence factors in, 2
Bacterial lipopolysaccharide (LPS), 127, 138
Bacterial transport, 109, 129
Bacteroides fragilis, 59, 81, 89–90, 104
Bartonella henslae, 70, 98, 154
Basidiobolus, 166
  B. ranarum, 165, 176
B cell response, 211, 240
BCG (Bacille Calmette-Guérin) vaccine, 212, 240
Blastomyces dermatitidis, 164, 174, 174*f*
Blastomycosis, 157, 168
Bordetella:
  B. bronchiseptica, 78, 86, 103, 107
  B. pertussis, 83, 106
Botulism toxin, 72, 100
Bovine spongiform encephalopathy (*see* Mad Cow Disease)
Branhamella, 74, 101
Brucella, 84, 106–107
  B. abortus, 78, 103
  B. melitensis, 63, 93
Bruton's agammaglobulinemia, 211, 228, 240, 250
Bubonic plague, 69, 97
Burkitt's lymphoma, 25, 49

C
C. coronata, 166
C. jejuni, 102–103
  enterocolitis, 65, 94

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Calcivirus, 51*t*
Campylobacter, 3
Candida albicans, 158–159, 161, 166, 169, 172, 175
  immunization and, 212, 240
Candidiasis, 155, 167, 175
  (*See also Candida albicans*)
Capnocytophyga, 74, 101
Cardiobacterium, 74, 101
CD4 glycoprotein, 222, 246
Cefoperazone, 124
Ceftriaxone, 124, 136–137
Cephalosporin, 124, 136
Chagas' disease (*see Trypanosoma cruzi*)
Chicken pox [*see* Varicella-zoster virus (VZV)]
Chlamydia, 141, 146, 149, 153
  C. pneumoniae, 85, 107, 146, 153
  C. psittaci, 143, 150
  C. trachomatis, 143, 145–146, 150, 152
  C. "TWAR," 146, 153
  developmental cycle of, 143, 151
Chloramphenicol, 120, 125, 135, 137
Cholera, 64, 76–77, 93, 103
Ciprofloxacin, 124
Clonal selection, 211
Clonorchis, 186, 186*f*–187*f*, 194, 202, 206
Clostridium:
  C. botulinum, 64, 94
  C. difficile, 61, 91
Coagglutination (COA), 235, 253
Coccidioides immitis, 159–160, 163, 171, 171*f*, 173
Coccidiomycosis, 157, 160, 168, 172
Complement, 224, 247
Complement-fixation (CF) test, 233, 251
Conjugation, 121, 135
Coronavirus, 8, 34
Corynebacterium diphtheriae, 66, 82, 95, 105
Counterimmunoelectrophoresis (CIE), 235, 253
Coxiella burnetii, 141, 148–149, 154
Coxsackievirus, 16, 41
Creutzfeldt-Jakob disease (CJD), 3, 12, 38, 41
Cryptococcosis, 155, 167, 175
Cryptococcus, 157, 167
Cryptosporidium, 178, 178*f*, 199
Cyclospora, 1, 69, 97, 178, 199
Cytokines, 221, 244
Cytomegalovirus (CMV), 17, 24, 26, 42, 44*f*, 48–49
  in neonates, 9, 19, 22, 36, 44, 47

D

Dengue fever, 2, 20, 46
Dermatomycoses, 175
Dermatophytosis, 158, 164, 169
DiGeorge's syndrome [*see* Thymic hypoplasia (DiGeorge's syndrome)]
Diphtheria, 82, 105
  (*See also Corynebacterium diphtheriae*)
Dipicolinic acid, 112, 131
Drechslera, 155, 155*f*, 167

E

E. coli, 69, 83, 97, 106
  enterohemorrhagic, 1
  freeze-fractured, 115, 115*f*, 122–123, 123*f*, 132, 136
  growth curves in, 119, 119*f*, 135
  penicillin in, 118, 134
  periplasmic space and, 110, 129
  porins in, 115, 132
Eastern equine encephalitis (EEE), 2, 11, 37
Echovirus, 8, 35
Ehrlichia, 2, 145, 151–152
  E. chaffeensis, 148, 154
ELISA [*see* Enzyme-linked immunosorbent assay (ELISA)]
Entamamoeba histolytica, 195, 207
Enterococcus, 65, 74, 94–95, 101
  E. faecium, 66, 95
  vancomycin-resistant, 1
Enterotoxin, 2
Enterovirus, 26, 49
Enzyme immunoassay, 236*f*, 237–238, 253–254
Enzyme-linked immunosorbent assay (ELISA), 216, 216*f*, 219–220, 236, 242–244, 253
Enzyme multiplied immunoassay test (EMIT), 235, 253

Epidermophyton floccosum, 163–165, 175
Epstein-Barr virus (EBV), 25, 48–49, 227, 249
(*See also* Infectious mononucleosis)
Escherichia coli (E. coli) (see E. coli)

F
Fifth disease, 16, 41, 226, 248
(*See also* Parvovirus)
Filobasidiella neoformans, 162, 173
Flavivirus, 39
Flukes (*see* Trematodes)
Francisella tularensis, 83, 106
Fungi, 165, 175
teleomorphs of, 162, 173
(*See also specific type*)

G
Gamma globulin, 20, 45
Gastroenteritis, 28, 50
pediatric, 27
Gel electrophoresis, 121, 121*f*, 122, 136
Gene cloning, 2, 118, 134
German measles virus (*see* Rubella virus)
Giardia, 1, 183, 196, 198, 201, 208–209
G. lamblia, 195, 207
life cycle of, 181, 181*f*, 200
Gonorrhea, 73, 101
Granuloma formation, 157, 168
Group B streptococci (GBS), 62, 62*f*, 63, 92–93

H
Haemophilus:
H. influenzae, 55, 65, 87, 94, 102
H. pneumonia, 58, 89
Hansen's disease, 56, 87
Hantavirus, 16, 41
Haplotypes, 212, 241
Hapten, 221, 245
Hapten-protein complex, 223, 247
Helicobacter, 3
H. pylori, 55, 70, 87, 98
Hemagglutinating antibody response, 214, 214*f*, 241
Hepatitis A (HAV), 27–28, 50
vaccine for, 23, 47
Hepatitis B (HBV), 13, 29, 39, 50
carriers of, 11, 37, 226, 248–249
diagnosis of, 234–235, 251, 252*t*
markers for, 11, 21, 37, 46
vaccine for, 23, 47
Hepatitis C (HCV), 3, 21, 28, 46, 50
Hepatitis D (HDV; delta), 8, 11, 13, 29, 34, 37, 39, 50
Hepatitis E (HEV), 10, 15, 29, 36, 41, 52
Herpes simplex virus (HSV), 5, 14, 33, 40
meningitis, in newborns, 8, 35
vaccine for, 23, 47
Histoplasma capsulatum, 159, 170, 170*f*
Histoplasmosis, 157, 168
HIV:
basic structure of, 32*f*
drugs, resistance to, 1
increased risk of, 14, 40
opportunistic infection and, 6, 33
(*See also* AIDS)
Human granulocytic ehrlichiosis (HGE), 144, 151
Human monocytic ehrlichiosis (HME), 142, 150
Human papillomavirus (HPV), 16, 18, 24, 26, 29, 36, 42–43, 48–49, 52

I
Idiotype, 231, 250
Imipenem, 124
Immunity, 221, 244–245
Immunodeficiency disorders, 228–229, 249–250
Immunoglobulin:
classes of, 2, 224–225, 247–248
structure of, 222, 245, 245*f*
Immunosuppression, 223, 246
Infantile X-linked agammaglobulinemia (*see* Bruton's agammaglobulinemia)
Infectious mononucleosis, 7, 20, 33, 46, 48, 238, 254
diagnosis of, 14, 19, 40, 45
Influenza, 30, 52, 85, 107
Haemophilus influenzae, 55, 65, 87, 94, 102
parainfluenza virus, 10, 31, 36, 53
vaccine for, 23, 47

Interferon, 7, 19, 34, 44–45
Interleukin 1, 222–223, 246
Isograft, 230, 250
Isotype, 230, 250

K
Klebsiella, 61, 91–92
Kuru, 12, 38

L
Lactobacilli, 81, 104
Latex agglutination (LA) test, 67–68, 96*t*, 236, 252
Legionella, 60, 75, 85, 91, 102, 107
Leprosy, 56, 87
Leuconostoc, 111, 130
Lice, 191, 204
Listeria, 56, 59, 87–88, 90
  bacterial meningitis and, 73, 100
  L. monocytogenes, 59
Löffler's medium, 80, 104
Lowenstein-Jensen medium, 80, 104
Lyme disease, 2, 71, 98, 116, 132–133, 193, 205–206
  treatment of, 76, 102
Lymphogranuloma venereum (LGV), 143, 145, 147, 150, 152, 154

M
Mad Cow Disease, 3, 15, 38, 40
Malaria, 192, 204
Malassezia furfur, 165, 175
Measles, 30, 36
  vaccine for, 23, 47
Megakaryocytes, 211
Meningitis, 221, 244
  aseptic, 10, 37
  bacterial, Listeria and, 73, 100
  Neisseria meningitidis, 84, 106, 127, 139
  in newborns, 8, 35
Methicillin-resistant *Staphylococcus aureus* (MRSA) (*See under Staphylococcus aureus*)
Microsporidia, 193, 206
Microsporum canis, 156, 164–165, 167, 174–175
Mitogenesis, 221, 244
Mitomycin, 114, 132
Mucor, 161, 172
Multiple myeloma, 232, 251
Mumps virus, 9, 22, 35, 47
Mycobacterium, 128, 138
  M. avium, 71, 99
  M. tuberculosis, 1
Mycoplasma, 141, 146–147, 149, 153
  M. pneumoniae, 57, 85, 88, 107

N
Nannizzia incurvata, 162, 173
Necrotizing fasciitis, 70, 98
Neisseria meningitidis, 84, 106, 127, 139
Nongonoccal urethritis (NGU), 142, 150
Norwalk virus, 28, 51*t*
Nosocomial pathogens, 1
Nucleic acid probes, 119, 134

O
Ornithosis, 142, 149
Ouchterlony agar-gel diffusion test, 217, 217*f*, 242
Oxygen, free radicals of, 3

P
Papillomavirus [*see* Human papillomavirus (HPV)]
Parainfluenza virus, 10, 31, 36, 53
Paramyxovirus, 9, 18, 30–31, 36, 43, 53
Parasites:
  fecal, diagnosis of, 195, 206–207
  raw fish consumption and, 182, 191, 200–201, 204
  (*See also specific type*)
Parvovirus, 5, 16, 32, 41–42
  (*See also* Fifth disease)
Pasteurella multocida, 61, 79, 92, 103
Pediculus humanus (*see* Lice)
Penicillin, 120, 124–125, 135, 137
Penicillinase, 109, 129
Penicillin-binding proteins (PBPs), 112, 131
Peptidoglycans, 2, 59, 90
Peroxidase, 111, 130
Pfiesteria piscicida, 182, 200

Phialophora verrucosa, 163, 173–174
Phthirus pubis (*see* Lice)
Piperacillin, 124
Plasmodium:
  life cycle of, 192*f*
  P. falciparum, 180, 180*f*, 185, 188*f*, 200, 202–203, 203*f*
Platelets, 211, 240
Pneumonia:
  atypical, 85, 107, 146, 238, 254
  Chlamydia pneumoniae, 85, 107, 146, 153
  Haemophilus pneumonia, 58, 89
  Legionella pneumophila, 60, 85, 91, 107
  Mycoplasma pneumoniae, 57, 85, 88, 107
  P. carnii pneumonia (PCP), 189–190, 203–204
  pneumococcal pneumonia, 75
  pneumonic plague, 69, 97–98
  Streptococcus pneumoniae, 1, 72, 100, 102, 128, 139
Polyacrylamide gel, 121, 136
Polyclonal hypergammaglobulinemia, 232, 251
Polymerase chain reaction (PCR), 116–117, 119, 126, 126*f*, 133–135
  process of, 127, 138
Precipitin curves, 215, 215*f*, 242
Prions, 3, 12, 15, 38, 41
Progressive multifocal leukoencephalopathy (PML), 30, 52
Pseudallescheria boydii, 157, 168
Pseudomembranous enterocolitis, 61, 76, 91, 102
Psittacosis, 142, 149

Q

Q fever, 141–142, 148–149
Quellung test, 72, 100
Quinolones, 58, 89, 124

R

Rabies, 12, 22, 38, 47
Respiratory syncytial virus (RSV), 14, 22, 30, 40, 47, 53
Reverse transcriptase enzyme, 18, 43
Rheumatic fever (RF), 71, 99
Rhinovirus, 12, 22, 38, 47
Rhizopus, 162, 173
  R. arrhizus, 166
Ribavirin, 8, 13, 35, 39
Rickettsiae, 141, 143–145, 148–154
Rocky Mountain Spotted Fever (RMSF), 144, 148, 151, 154
Rotavirus, 17, 24, 27, 42–43, 48, 51*t*
Rubella virus, 7, 12, 34, 38, 238, 254
  pregnancy and, 15, 40

S

Salmonella, 65, 94, 189, 203
  S. enteritidis, 112, 131
Scabies, 192, 205
Scarlet fever, 238, 254
Scatchard plot, 217–218, 218*f*, 243
Schistosoma:
  S. haematobium, 194
  S. japonicum, 194
  S. mansoni, 194
Schistosomiasis, 193, 196, 205–206, 208
Serum electrophoretic profiles, 231, 231*f*, 232, 250–251, 251*f*
Sheep blood agar, 80, 104
Shigella, 73, 101
Shingles, 38 [*See under* Varicella-zoster virus (VZV)]
Siderophores, 110, 129
Smallpox, 12, 39
Southern blot, 117, 126, 134, 138
Spore, thick-walled, 156, 156*f*, 167
Sporothrix schenckii, 158, 168
Sporotrichosis, 155, 167
St. Louis encephalitis, 13, 18, 39, 43–44
Staphylococcus aureus, 2, 15, 41, 64, 66, 94–95, 97
  enterotoxin, 64, 93
  methicillin-resistant (MRSA), 1, 68
  in toxic shock syndrome, 67, 95–96
  vancomycin-indeterminate (VISA), 1, 58, 89
Staphylococcus epidermis, 80, 104
Streptococcal pharyngitis, 76

Streptococcus:
α-hemolytic, 81, 104
group A, 127, 139
group B (GBS), 62, 62*f*, 63, 92–93
[*See also* Group B streptococci (GBS)]
S. mutans, 81, 105
S. pneumoniae, 1, 72, 100, 102, 128, 139
S. pyogenes, 84, 106
S. salivarius, 82, 105
Strongyloides, 191, 195, 204, 207
Subacute sclerosing panencephalitis virus (SSPE), 17, 42–43, 212, 226, 241, 249
Sulfonamide, 120, 135
Superoxidase dismutase, 3, 110–111, 129–130
Swiss-type hypogammaglobulinemia, 228, 232, 250–251
Syphilis, 59–60, 63, 90, 93, 239, 255

T
Taenia:
T. saginata, 182–183, 200–201
T. solium, 178, 200
T cells, 221, 245
Tetanus, 73, 101
Thayer-Martin (TM) agar, 79, 103
Thienamycin, 124
Thiosulfate citrate bile salts sucrose medium, 79, 104
Thymic hypoplasia (DiGeorge's syndrome), 229, 250
Tick-borne encephalitis virus, 30
Tinea:
t. capitis, 165, 175
t. corporis, 164, 175
t. cruris, 164
t. pedis, 165, 175
t. versicolor, 165, 175
Tolerance, immunologic, 222, 246
Toxic shock syndrome, 2, 67, 95
Toxoplasma, 25, 49, 179, 183, 196, 199, 201, 207
AIDS and, 184, 184*f*, 201
Trachoma, 143, 145–146, 150, 152
Transduction, 121, 135
Transformation, 121, 135
Transient aplastic crisis, 5, 32
Trematodes, 194, 197, 206, 208
(*See also specific type*)
Trichinosis, 196–197, 208
Trichomonas vaginalis, 197, 208
Trichuris, 207
Trimethoprim (TMP), 125, 137
Trypanosoma cruzi, 184, 202
Tuberculosis, 58, 73, 88, 100
M. tuberculosis, 1
Tularemia, 83, 106

V
Vaccines, 23, 47
Vancomycin-indeterminate *Staphylococcus aureus* (VISA) (*See under Staphylococcus aureus*)
Varicella-zoster virus (VZV), 27, 49–50
chicken pox and, 24, 48, 219, 226, 243, 248
shingles and, 11, 37–38
Venereal disease, 59–60, 72, 90–91, 99
(*See also specific type*)
Vibrio:
V. cholerae, 55, 87
V. parahaemolyticus, 77, 103
V. vulnificus, 77, 103
Viruses, cytopathic effects of, 19, 45
Visceral larva migrans, 197, 208

W
West Nile virus, 3, 29–30, 52
Wiskott-Aldrich syndrome, 229, 250

X
Xenograft, 229, 250

Y
Yersinia:
Y. enterocolitica, 78, 103
Y. pestis, 69

Z
Zygomycosis, 165–166, 175–176